THE NUCLEOPHILIC SUBSTITUTION OF VARIOUS CHLOROANTHRAQUINONES AND THEIR POSSIBLE REARRANGEMENT VIA ARYNE INTERMEDIATES

by

Edward H. Ruediger, B.Sc.

A thesis

submitted in partial fulfillment

of the requirements for the degree of

Master of Science

Brock University

St. Catharines, Ontario

January, 1977

Acknowledgements

I would like to express my appreciation to Dr. M. S. Gibson for his guidance, encouragement and optimism during the course of this work.

I would also like to thank Dr. P. Bickart, Dr. J. Clark and Mr. Ian Brindle for useful discussions. Special thanks must go to Mr. Tim Jones for the mass and n.m.r. spectra and to the technical staff of Brock University, especially Mr. John Vandenhoff.

I am indebted to my fellow graduate students who never lost their sense of humour and always added a cosmopolitan flavour to every endeavour.

My thanks are also due to Miss Janet Hastie for the typing of this thesis and the Ontario Government for several graduate scholarships.

To my parents—

for their patience

"...the organic chemist...should not be surprised if his predictions in a new situation turn out to be erroneous. It is frequently difficult to anticipate all the factors which may be critical in any given situation."

--A. Corwin and M. Bursey

(from "Elements of Organic Chemistry")

CONTENTS

ABSTRACT

The work in this thesis deals mainly with nucleophilic substitution of chloroanthraquinones as a route to various starting materials which might rearrange, via aryne intermediates to afford fused-ring heterocylic carboxylic acids.

1-Amino-5-chloroanthraquinone was successfully prepared by reacting 1,5-dichloroanthraquinone with sodium azide in refluxing dimethylsulfoxide (DMSO). It could also be prepared from the same starting material by reaction with ammonia (gas) in DMSO in the presence of potassium fluoride. Treatment of 1-amino-5-chloroanthraquinone with potassium amide in liquid ammonia or with potassium t-butoxide in t-butylbenzene returned mainly starting material, although in the latter case some 1-amino-5-hydroxy-anthraquinone was also isolated.

1-Hydroxy-5-chloroanthraquinone was ultimately prepared by diazotization of the amino-analog. It was recovered almost quantitatively after treatment with potassium amide in liquid ammonia. The reaction with potassium t-butoxide in t-butylbenzene was anomalous and gave 1-hydroxyanthraquinone as the only isolable product.

Acridines were successfully prepared by the action of 70% sulfuric acid on 1,5-bis(p-toluidino)-anthraquinone and 1-p-toluidino-5-chloroanthraquinone, and in the latter case, cleavage to give an acridine-carboxylate was attempted.

Substituted anthraquinones reacted with sodium azide in sulfuric acid to give azepindiones by -NH insertion. Methods for separating and

identifying isomeric mixtures of these compounds were examined. Attempted decarbonylation of selected azepindiones to give acridones gave mainly what were thought to be amino-benzophenone derivatives.

Chloroanthraquinones were found to react with hexamethylphosphoramide (HMPA) to give mixtures of the dimethylamino- and methylamino-derivatives. Under the same conditions halogeno-nitrobenzenes and nitrophenols were substituted to give the appropriate dimethylamino-benzenes, except in two cases. 3-Chloronitrobenzene reacted anomalously to give a small amount of 3,3'-dichloroazobenzene and a trace of 4-dimethylamino-nitrobenzene. Pentachlorophenol reacted to give a pentachlorophenylphosphorodiamidate in good yield.

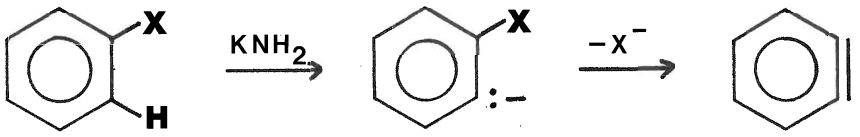
INTRODUCTION

The formation of aryne from ortho-anionized benzene derivatives

Since the general acceptance of benzyne (aryne) as an actual intermediate there have been a number of reviews concerned with its chemistry. A good introductory review was offered by Bunnett in 1961.[1] A much more thorough monograph[2] has been published since on the generation and reactions of arynes.

In general the hydrogens ortho to the halogen in aryl halides are considerably more acidic than the other ring hydrogens. This was substantiated by reactions done with various o-deuterobenzene derivatives and sodium amide in liquid ammonia, which indicated that exchange was most rapid in the 2-position.[3]

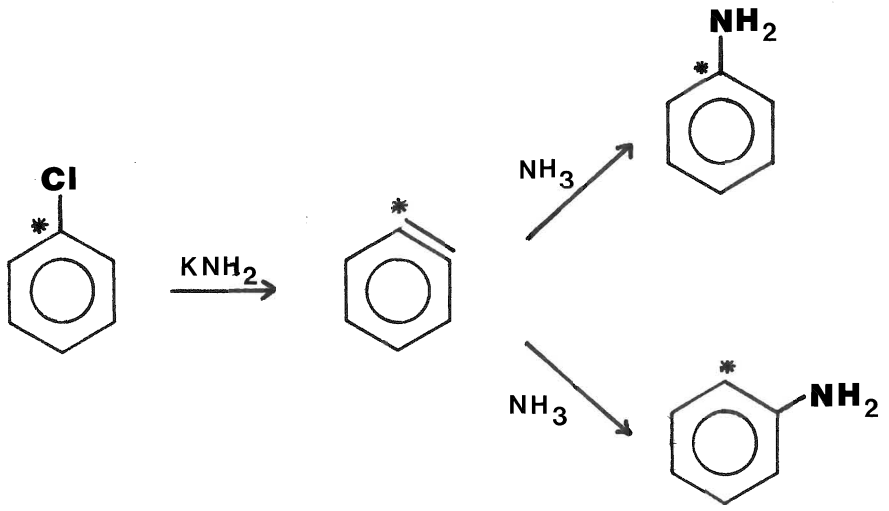
Thus, aryl halides may be ortho-anionized by the action of a very strong base (e.g., KNH_2), and subsequent loss of halide ion generates an aryne (benzyne).



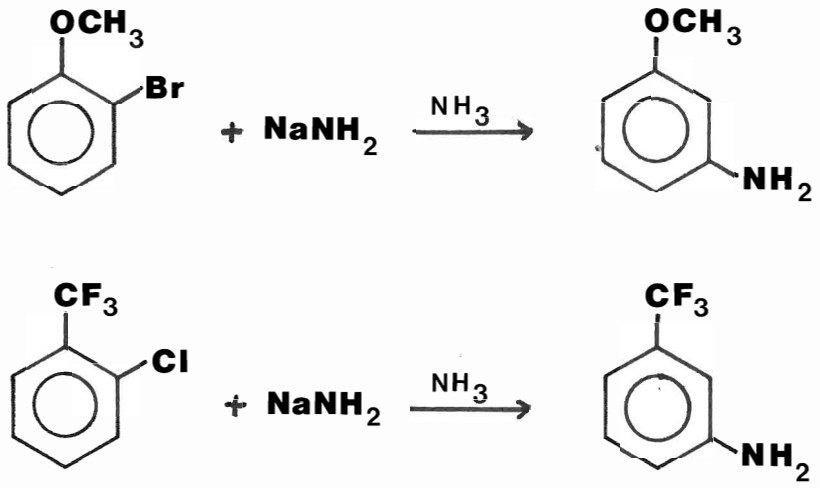
As would be expected for this type of mechanism, halogenobenzenes lacking o-hydrogens are unreactive under these conditions.[4]

Arynes (benzynes) are short-lived species which, once produced, will usually react with a nucleophile and a proton, although other types of reaction are possible.

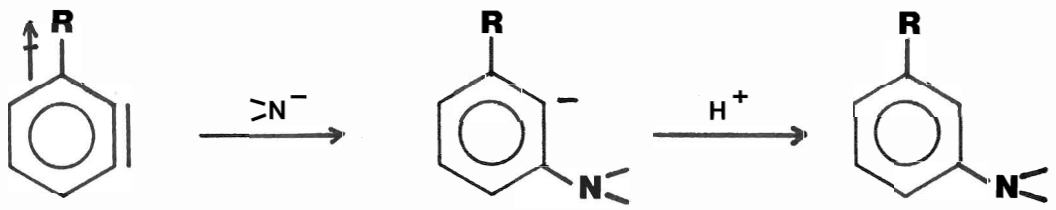
Although aryne-type intermediates had been proposed quite early[5,6] to account for a number of aromatic rearrangements, it was the decisive experiment by Roberts, et al.[7] which fostered general acceptance of the aryne hypothesis. The previously known reaction of halogenobenzenes (except fluorobenzene) with sodium amide in liquid ammonia to give aniline[8] was performed using chlorobenzene-1-^{14}C. Roberts and co-workers showed that the reaction gave equal amounts (after correcting for a $^{12}C/^{14}C$ isotope effect) aniline-1-^{14}C and aniline-2-^{14}C and consequently proposed the following mechanism.



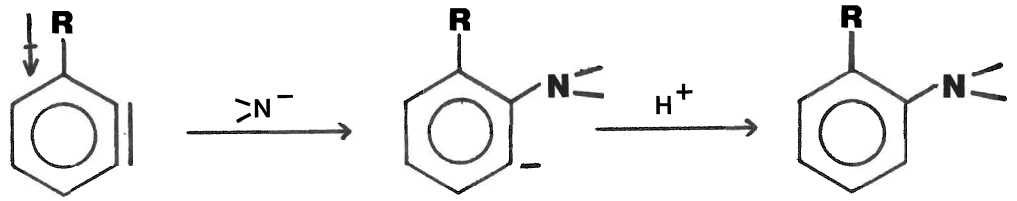
The following two reactions, which had been reported by Bergstrom et al.[8], left the criteria for nucleophilic additions to unsymmetrically substituted arynes open to question, since both $-OCH_3$ and $-CF_3$ proved to be m-directing.



Roberts and co-workers[9] proposed that addition of the nucleophile was controlled by the inductive effect of the substituent. Thus, the inductive effect would direct the approaching nucleophile into such a position that the resulting negative charge is best stabilized by the substituent. Since both $-OCH_3$ and $-CF_3$ are inductively electron-withdrawing, this explanation is consistent with the products observed. This is illustrated below where in (I) R is an inductively electron-attracting substituent and in (II) R is electron-releasing.



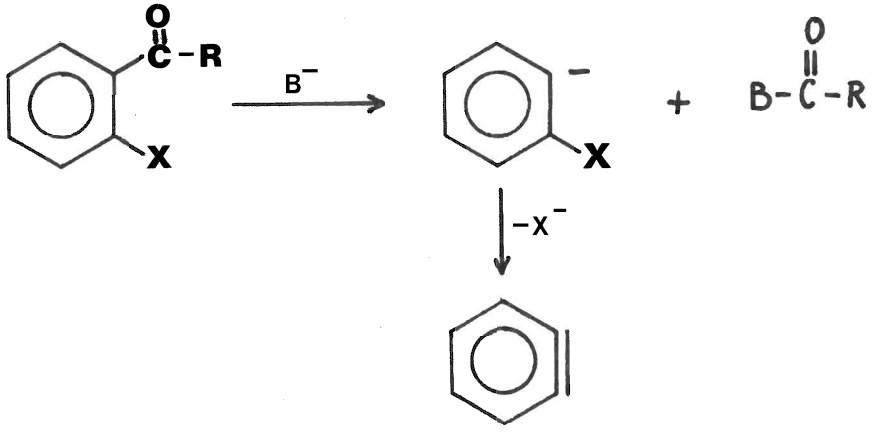
I



II

The rearrangements which may occur in these elimination-addition reactions are sometimes useful in affording positional isomers which may not be available by other synthetic routes.

There are a number of other means of generating o-halogenophenyl (aryl) anions. One method, which is of particular interest in this work, is the alkaline cleavage of non-enolizable ketones, or the so-called Haller-Bauer cleavage[10]. Here cleavage of 2-halogenophenyl ketones leads to a 2-halogenophenyl anion which may then lose halide ion to form benzyne.

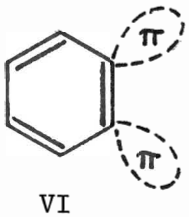


A number of structures (III-VII) have been proposed for benzyne.

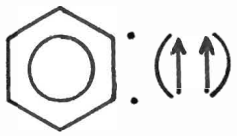
III

IV

V



VI



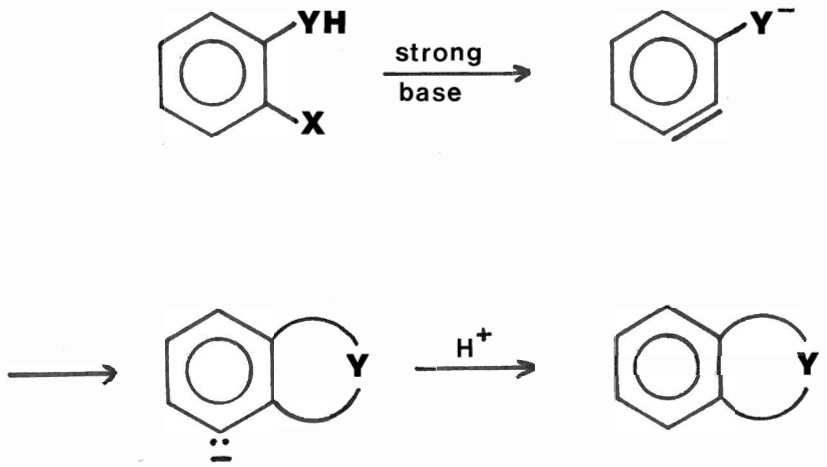
VII

Formula VII represents a diradical where the two unpaired electrons have parallel spins. However, benzyne shows no reactions characteristic of radicals[1] and so this alternative is discarded.

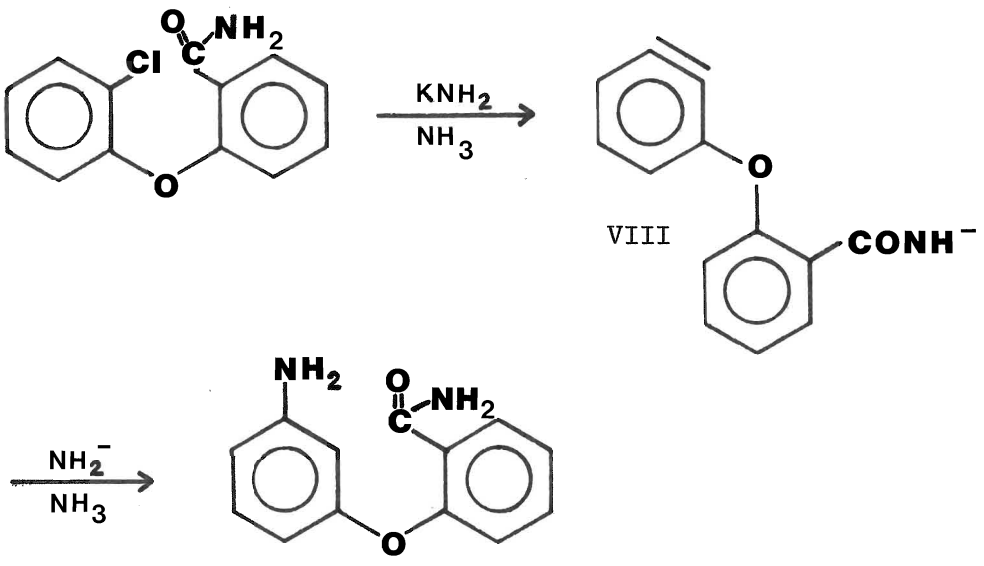
(VI) implies that benzyne has two π-orbitals at an angle of 60°, which suggests only weak overlap of these orbitals. In fact, overlap occurs to a larger extent to form a weak bond[2]. This is better represented by (III), but unfortunately this structure is misleading in that it implies the presence of an actual triple bond and neglects the resonance form (IV) which leads to a bond order of 2.5. Actually, benzyne contains a nearly unperturbed aromatic system with a weak extra bond in the orthogonal plane. This is best represented by (V) and this form will be used throughout this thesis.

Ring closures via aryne intermediates

A variety of nucleophiles add readily to arynes. If the nucleophile in question is part of a side-chain which is attached to the aryne, an intramolecular addition can result in ring closure as shown below.

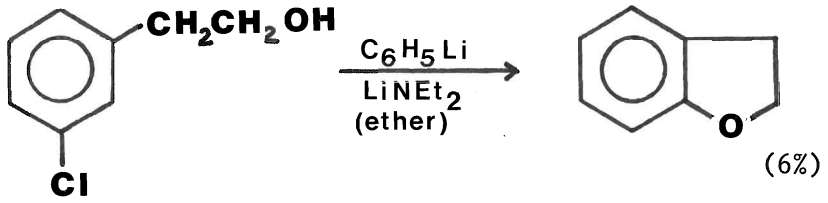


A problem associated with this type of reaction is that the side-chain nucleophile may not be able to compete effectively with the external base. With potassium amide in liquid ammonia as base, amination products are frequently isolated as by-products in ring closure reactions[11,12]. In the example below, it is probable that the preferred conformation of the intermediate (VIII) leaves the side-chain nucleophile too far from the aryne to compete with amide ion addition[13].



(55%)

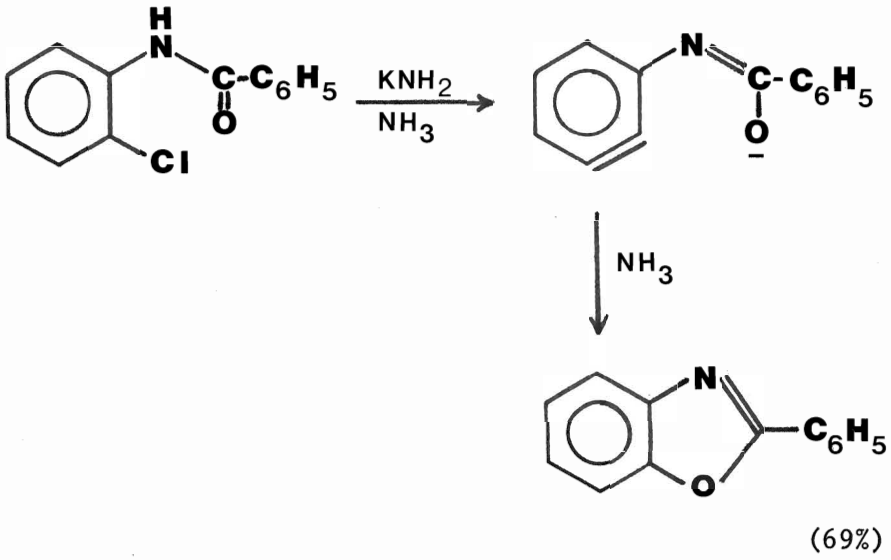
Occasionally, intramolecular nucleophilic addition will occur in certain arynes (for steric reasons) although the same nucleophile could not compete with the base present in a bimolecular addition under the same conditions. Thus, alkoxides will not add to an aryne in the presence of various lithium amides (in ether)[14], but if the alkoxide is part of a side-chain, ring-closure will occur in modest yield.



(6%)

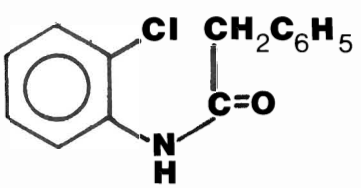
The side-chain nucleophiles used in these types of ring closures have included carbon, oxygen, nitrogen and sulfur functional groups. A number of new syntheses for fused-ring heterocycles have been developed using this approach[15-17].

e.g.,

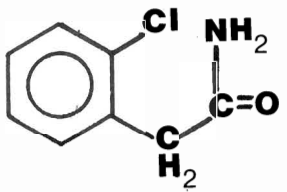


(69%)

Limitations to these reactions have been found. Kato[18] found that (IX) and (X) were recovered unchanged from treatment with potassium amide in liquid ammonia.



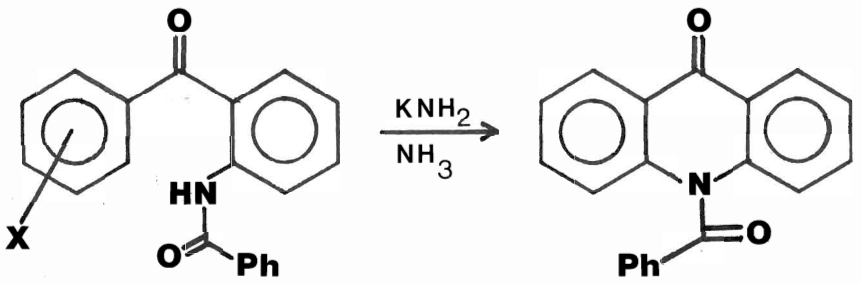
IX



X

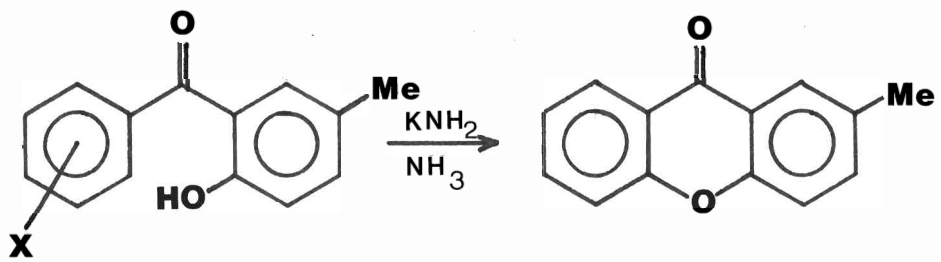
Interestingly, however, the N-methyl derivative of (IX) cyclized readily under the same conditions in 91% yield. The observations were explained[1] by noting that the strong base probably initially removed a proton alpha to the aromatic ring and transformed it to an anionic centre which (through resonance with the ring) decreased the acidity of the ring hydrogens sufficiently that they were not susceptible to attack by amide ion.

Recently, acridone syntheses have been reported[19] using a ring closure which presumably proceeds via an aryne intermediate.

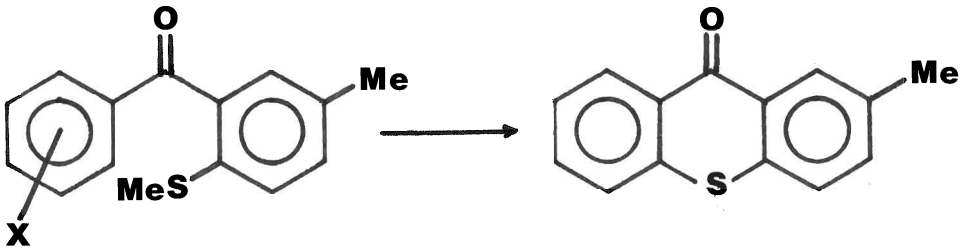


(67%)

Similarly a series of appropriately substituted benzophenones have been converted to xanthones and thioxanthones by the action of potassium amide in liquid ammonia[20].



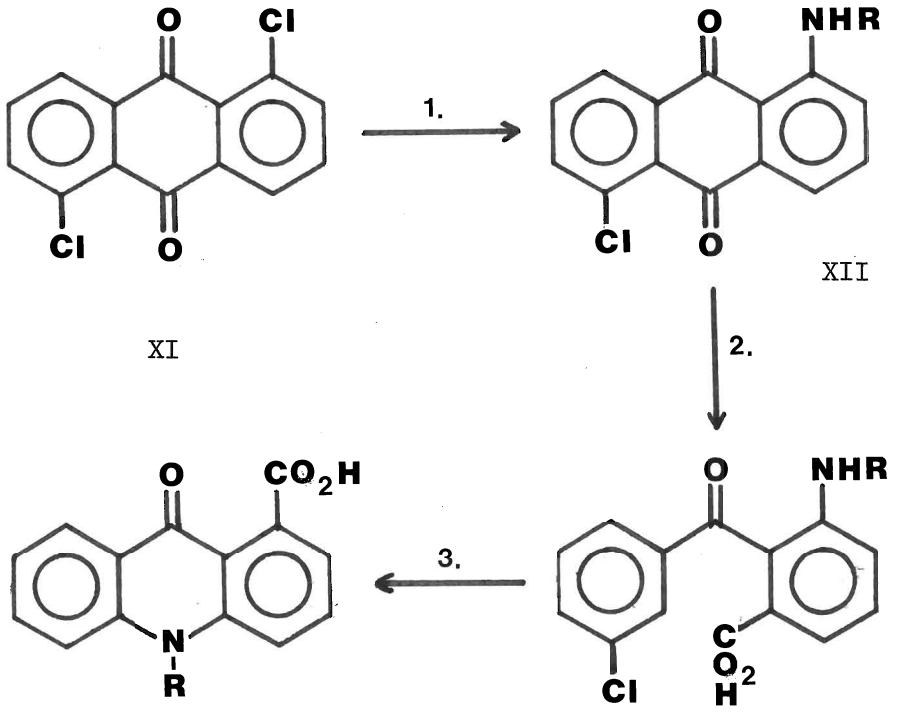
X = 2- or 3-chloro(bromo) (14-66%)



X = 3-chloro (17%)

Acridone synthesis via reaction of anthraquinones through a benzyne intermediate

The work in this thesis was initially conceived to explore a route to acridone derivatives via benzyne intermediates as shown below.

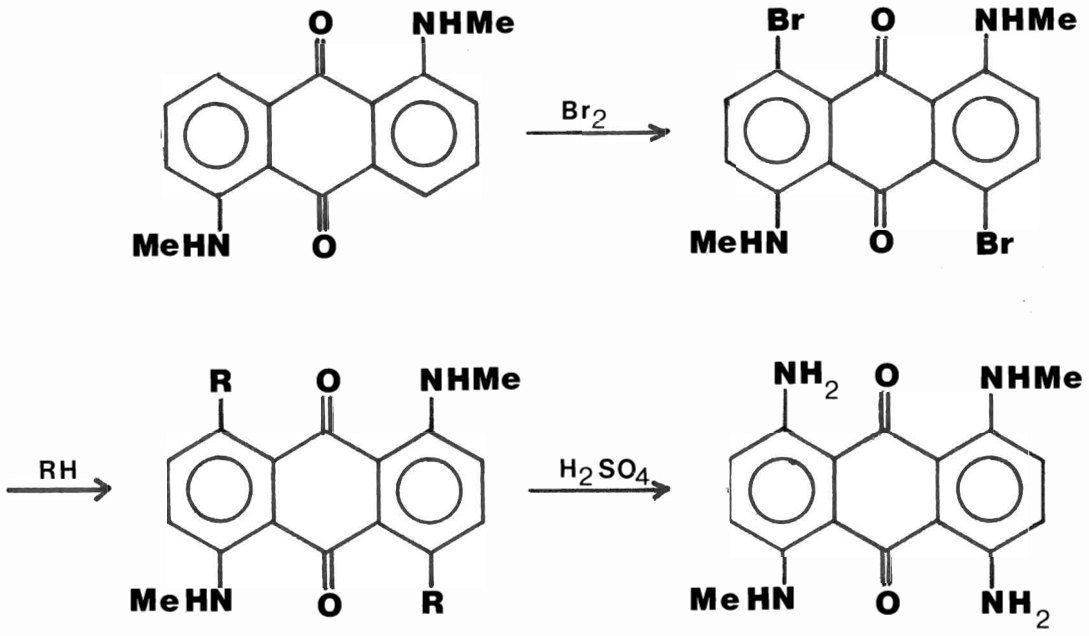


XIV XIII

This route has proven successful in affording (XIV) where R = Me[21] but this work will attempt to obtain (XIV) where R = H. Methods for introducing amino-groups into an anthraquinone system (step 1) and for cleavage of anthraquinones are discussed below. Success in this scheme depends on an intramolecular cyclization (step 3) taking precedence over complete cleavage after step 2.

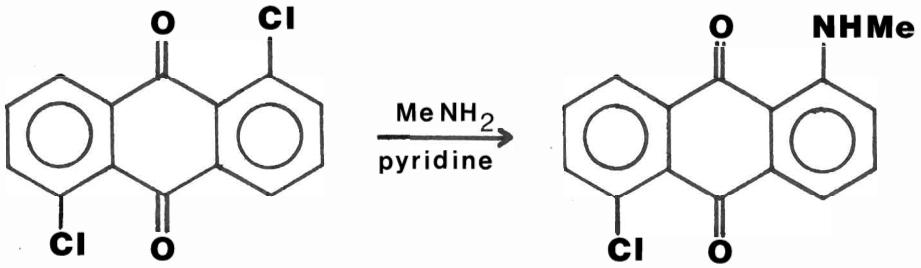
Introducing amino-groups into the anthraquinone system

A number of varied methods of introducing nitrogen-containing nucleophiles into the anthraquinone system have been reported. Hall and Hey[22] were able to synthesize (XV) and (XVI) using p-toluenesulfonamide and methylamine, respectively, as the nucleophiles.



XV

R = $-NHSO_2-C_6H_4CH_3$



XI XVI

Dimethylformamide (DMF) has been used in preparing dimethylamino-anthraquinones from halogeno-anthraquinones but Lord and Peters[23] have reported the formation of N-methylaminoanthraquinones in instances where longer reaction times were used. Later,[21] a more convenient route to N-methylaminoanthraquinones by the action of N-methylformamide on chloroanthraquinones was reported. However, an attempt to obtain amino-anthraquinones from chloro-anthraquinones in refluxing formamide was unsuccessful and gave mainly chloro-anthracenes, presumably by a Leuckart-type reaction[21].

Amino- and alkylamino-anthraquinones have also recently been reported as the products of the photochemical substitution of methoxy-anthraquinones with amines[24]. The best yields were obtained when 1-methoxyanthraquinone was irradiated in acetonitrile: water (1:1) containing ammonia or methylamine to give 1-aminoanthraquinone (96%) and 1-methylaminoanthraquinone (81%), respectively.[24]

Lord and Peters were able to prepare 1-anilino-anthraquinone (73%), together with numerous by-products, by an Ullmann condensation of

aniline with 1-chloroanthraquinone[25]. More recently they have also obtained a number of other 1-arylaminoanthraquinones by similar condensations with the appropriate arylamines[26]. The condensation of 1-chloroanthraquinone with 4-aminopyridine was unique, in that 1-hydroxyanthraquinone (5.9%) and 1-aminoanthraquinone (37.8%) were obtained together with the expected 1-(4-pyridylamino)-anthraquinone.

Other workers have reported a more convenient method of producing 1-amino-4-arylaminoanthraquinones[27], under much milder conditions than Ullmann-type condensations. 1-Amino-4-chloro(bromo)anthraquinone was added to a mixture of aniline and aluminum chloride at 0° and the mixture was then maintained at 20° for one hour. Chromatography gave 1-amino-4-anilinoanthraquinone (85%) and some starting material was returned. The reaction is limited, in that it requires a free amino-group in the 1-position, since 1-benzamido-4-chloro-anthraquinone fails to react[27].

The development of the present work has led to the examination of other methods involving (a) use of sodium azide and (b) use of hexamethylphosphoramide (HMPA) for introducing nitrogen functionality into anthraquinones. The background to these reactions will be covered after consideration of the cleavage of anthraquinones.

Cleavage of anthraquinones by the action of base

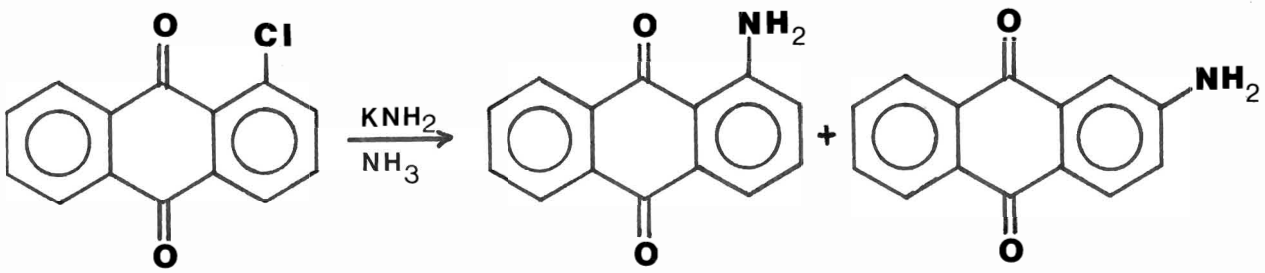
Although anthraquinones are more resistant to basic cleavage than other non-enolizable carbonyl compounds, Davies and Hodge[28] have reported that 1- and 2-chloroanthraquinone and a series of methoxy-anthraquinones were cleaved in high yield by an excess of potassium t-butoxide:water

(molar ratio, 10:3) in 1,2-dimethoxyethane at ca. 85°. This work was later extended to the cleavage of methyl ethers of some naturally occurring hydroxy-anthraquinones[29].

Anthraquinones can, in principle, be cleaved by this reagent in four ways yielding a mixture of benzoic acids and/or phthalic acids and a non-acidic fragment (Scheme 1).

In fact, it was found that the cleavage of 1-chloroanthraquinone gave an acidic fraction (96%) containing benzoic (23%), 3-chlorobenzoic (32%) and phthalic (45%) acids. 2-Chloroanthraquinone was cleaved (97%) to give benzoic acid (39%), a mixture of 3- and 4- chlorobenzoic acids (39%) and phthalic acid (22%).

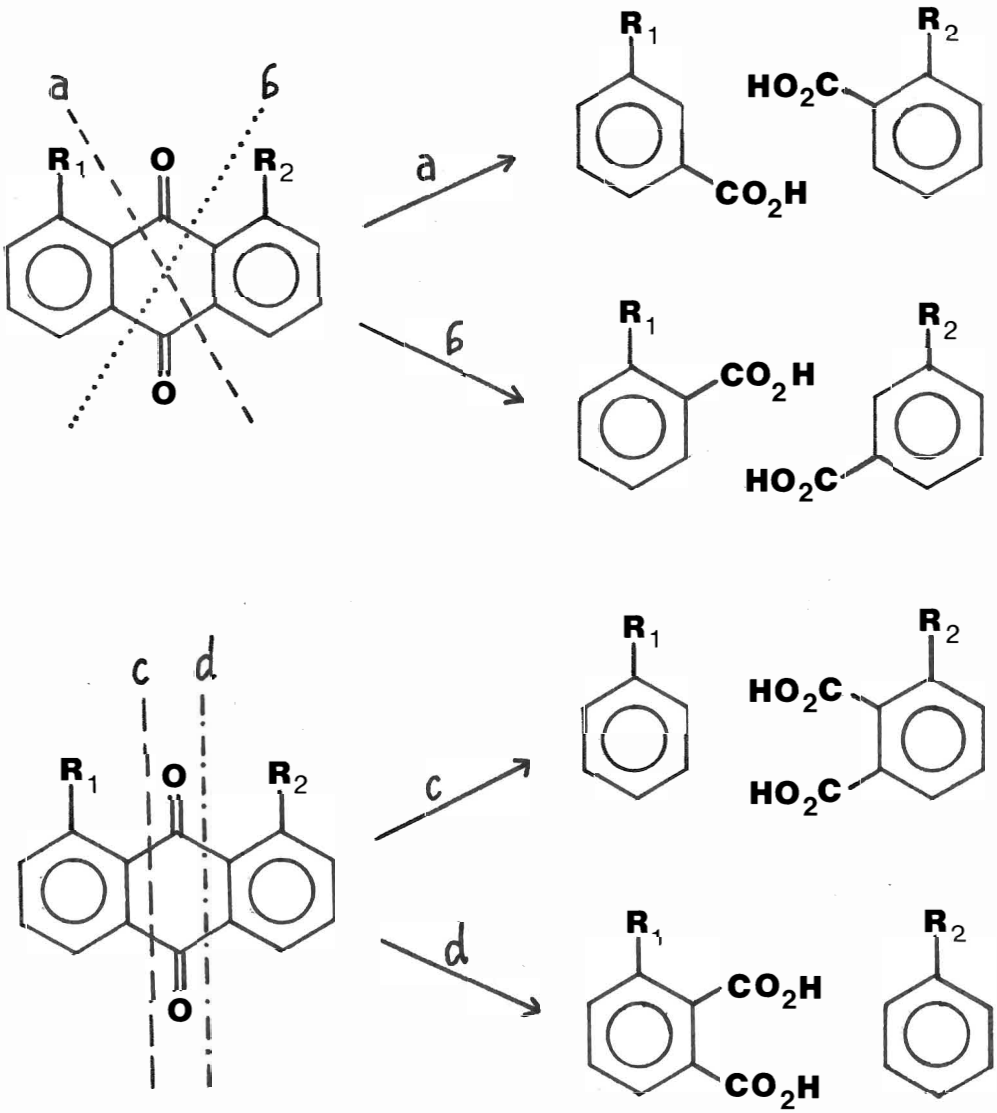
It is interesting to note that 1-chloroanthraquinone gave no apparent cleavage when reacted with potassium amide in liquid ammonia[30], but gave instead 1- and 2-aminoanthraquinones. 2-Chloroanthraquinone was returned almost quantitatively under similar conditions[30].



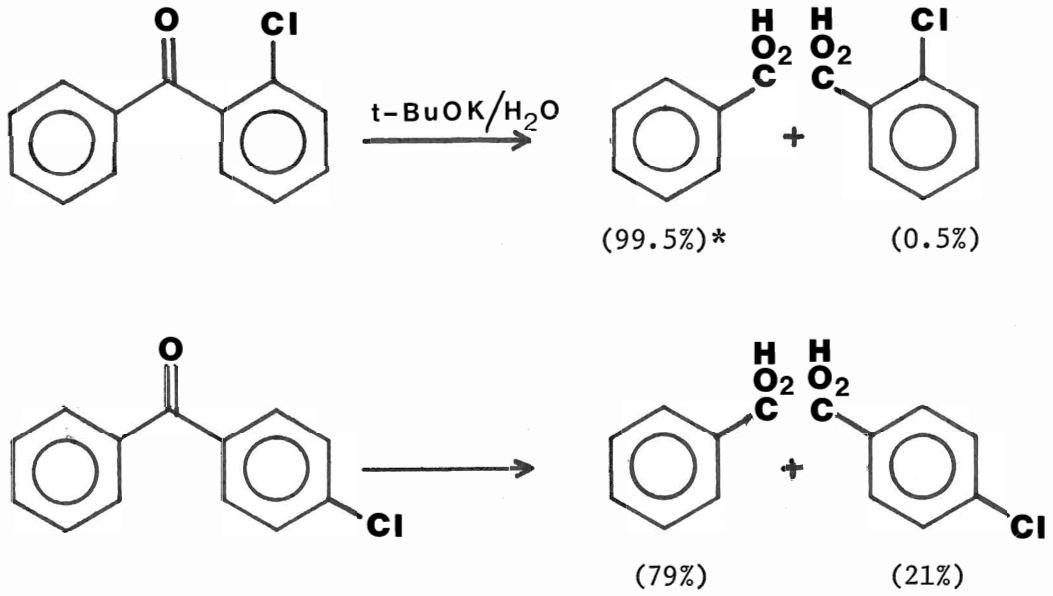
(49%) (17%)

Earlier work done by Davies and Hodge[31] showed that benzophenones could also be cleaved by the potassium t-butoxide-water reagent in good

SCHEME 1[28]


a
b
R1
O
R2
O
a
b
R1
HO2C
CO2H
R2
R1
CO2H
R2
HO2C
c
d
R1
O
R2
O
c
d
R1
HO2C
HO2C
R2
R1
CO2H
CO2H
R2

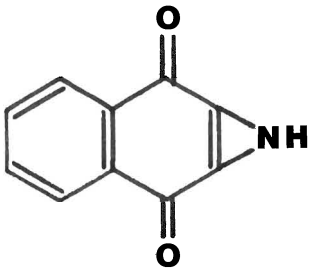
yield at 20°. It was found that substituted benzophenones were cleaved more readily than unsubstituted benzophenone and that the bond closer to the substituent was preferentially cleaved with the preference for such cleavage being greatest for 2-monosubstituted benzophenones and least for 4-substituted benzophenones[31].



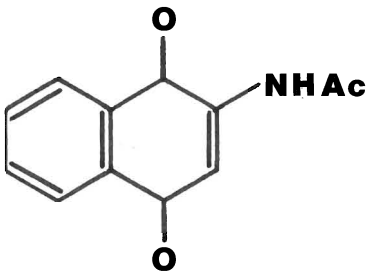
*percentages represent the composition of the acid fractions obtained.

The reaction of quinones with sodium azide

In 1924 Korczynski[32] observed the reaction of α-naphthaquinone with hydrazoic acid to give a compound of composition $C_{10}H_5O_2N$. He proposed the structure (XVII).

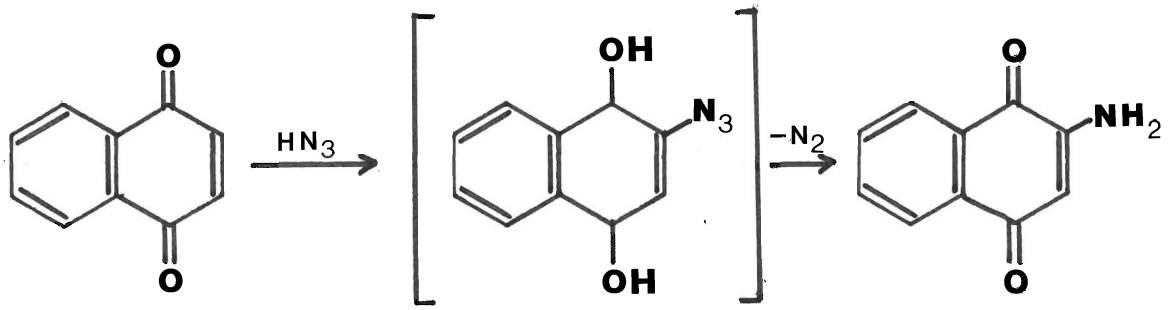


XVII



XVIII

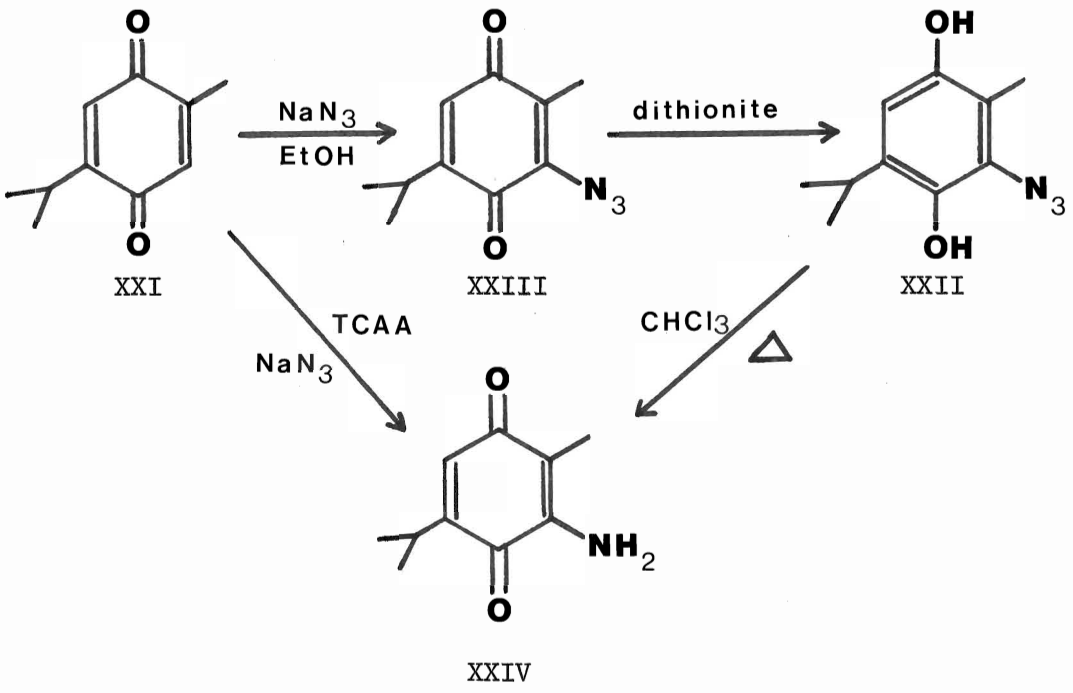
Fieser and Hartwell[33] later re-examined the reaction and obtained (XVIII) by reductive acetylation of what had previously been identified as (XVII). However, careful purification and analysis showed that the initial product was, in fact, 2-amino-1,4-naphthaquinone (XX). The following mechanism was proposed,



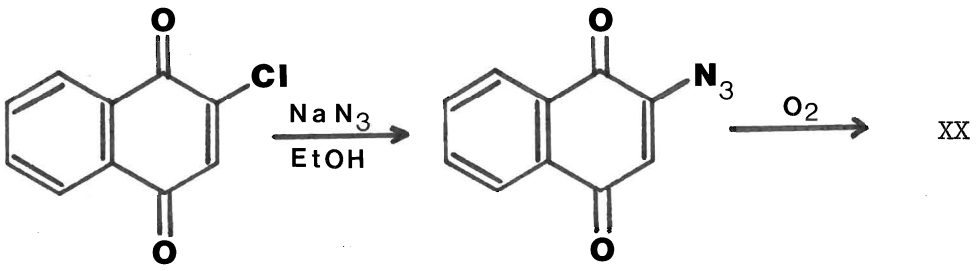
XIX XX

although the intermediate hydroquinone (XIX) could not be prepared to check this hypothesis. It was not until much later that work done by Moore and Sheldon[34] on thymoquinone (XXI) established a hydroquinone as an intermediate in this type of a reaction. The appropriate hydroquinone (XXII) was prepared by dithionite reduction of 3-azidothymoquinone

(XXIII) and was found to give the amine (XXIV) almost quantitatively on refluxing in chloroform under an argon atmosphere.

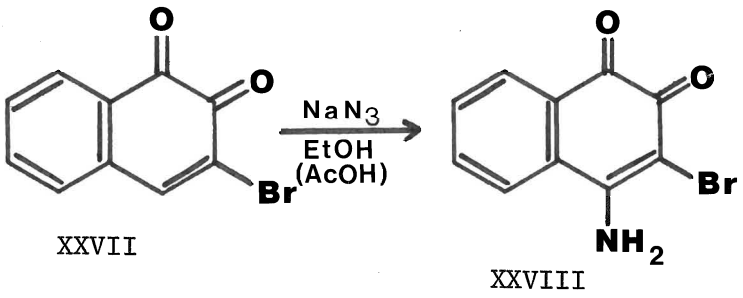


The reaction of 2-chloro-1,4-naphthaquinone (XXV) with sodium azide in refluxing aqueous ethanol gave 2-azido-1,4-naphthaquinone (XXVI) which was reported to give (XX) on air oxidation[2], although no mechanism was forwarded.



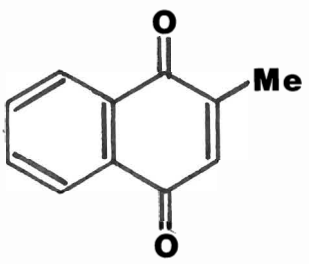
XXV XXVI

Surprisingly, 3-bromo-1,2-naphthaquinone (XXVII), on treatment with sodium azide in ethanol or glacial acetic acid gave no halogen replacement but instead gave 3-bromo-4-amino-1,2-naphthaquinone (XXVIII)[33].

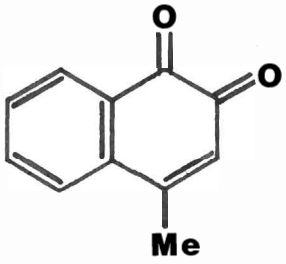


XXVII XXVIII

However, in the case of 2-methyl-1,4-naphthaquinone (XXIX) and 4-methyl-1,2-naphthaquinone (XXX) there was no reaction, presumably due to the blocking of addition by the methyl groups[33].

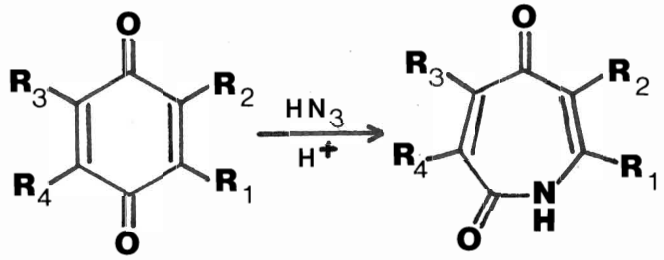


XXIX



XXX

Later work by Folkers et al.[35,36] showed that using different conditions led to a different type of reaction with (XXIX) and other substituted quinones. Various quinones were reacted with sodium azide in concentrated sulfuric acid at 0°. Their results are summarized below:

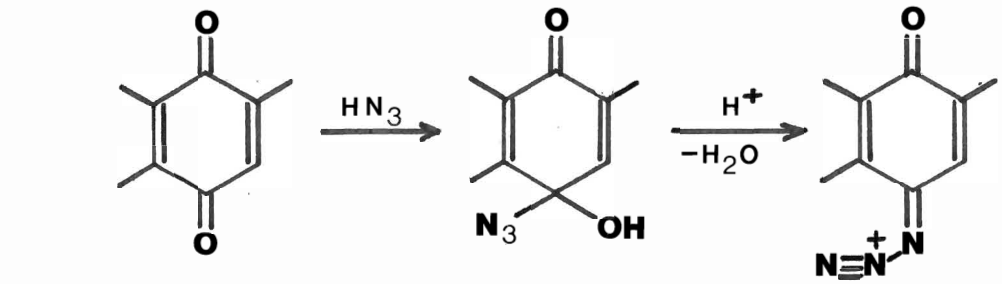


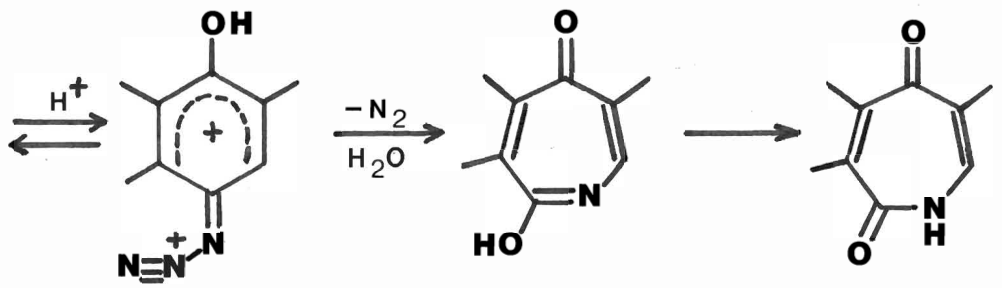
XXXI XXXII

	R_1	R_2	R_3	R_4
(a)	H	Me	Me	Me
(b)	H	$CH(Me)_2$	H	Me
(c)	H	Me		
(d)	H	Me	H	Me
(e)	Me	Me	Me	Me

The reaction, which is basically a Schmidt-type reaction, was said to give -NH insertion at the least hindered carbonyl so that the nitrogen is attached to the least substituted carbon, to afford the azepindione (XXXII).

The reaction was presumed to occur as follows:





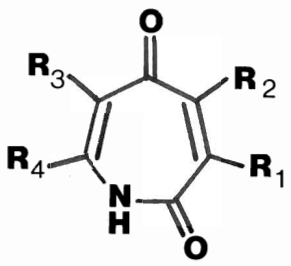
XXXIII

The protonated intermediate (XXXIII) loses nitrogen in a trans displacement by the migrating group. In unsymmetrical quinones the migrating group was thought to be the one with the least positive charge density (i.e., the least substituted carbon). The identification of the compounds obtained was based on n.m.r. decoupling experiments[35] which

supposedly indicated that the -NH proton was directly coupled to a =CH proton (i.e., they are adjacent).

Subsequent study of these reactions[37,38], however, showed the previous identification to be in error.

Reinterpretation of n.m.r. data and the identification of the products of alkaline hydrolysis of the azepindione[37] showed that the structure was not (XXXII) but (XXXIV).



XXXIV

Later work done on acidic and basic derivatives of (XXXIV)[39] (and their therapeutic value) was consistent with this structure assignment.

This is consistent with the belief[40] that the Schmidt reaction is mainly sterically controlled. The least hindered carbonyl is preferentially attacked, followed by preferential migration of the larger adjacent group. The n.m.r. spectra were complicated by long range couplings and particularly by cross-carbonyl coupling[41] in the system =CHCONH-. This deceived previous workers into assuming that the amido and vinylic groups were adjacent.

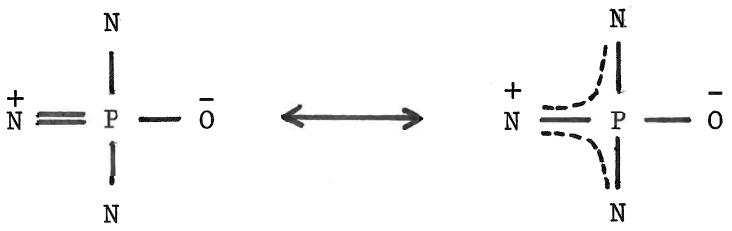
Since the largest segment done in this thesis involves the introduction of nucleophiles onto an anthraquinone skeleton, it was thought to be worthwhile to investigate possible reactions of sodium azide with chloroanthraquinones. The products of these reactions would then be considered as possible intermediates for acridone synthesis.

Nucleophilic displacements using hexamethylphosphoramide (HMPA)

Triamides of orthophosphoric acid have been prepared by the reaction of phosphorus oxychloride with an excess of secondary amine[42]. The reaction with dimethylamine gives hexamethylphosphoramide (HMPA).

$$OPCl_3 + 6HN(CH_3)_2 \longrightarrow OP[N(CH_3)_2]_3 + 3\ H_2N(CH_3)_2^{+}Cl^{-}$$

The double bond character of the P-O bond indicates 50% ionic character[43]. A structure with symmetrical distribution of positive charge (XXXV) over the $P(N)_3$ grouping has also been proposed[44].

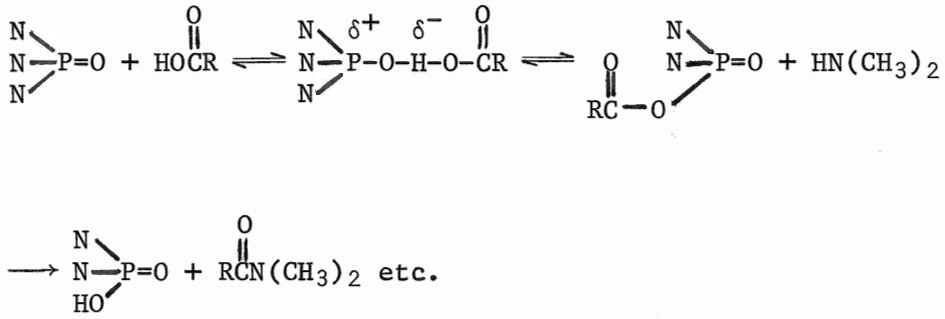


XXXV

The resulting high electron-density on the oxygen accounts for the large dipole moment and high basicity of HMPA.

These properties, together with a large liquid range and high boiling point, make it a particularly effective polar aprotic solvent[45].

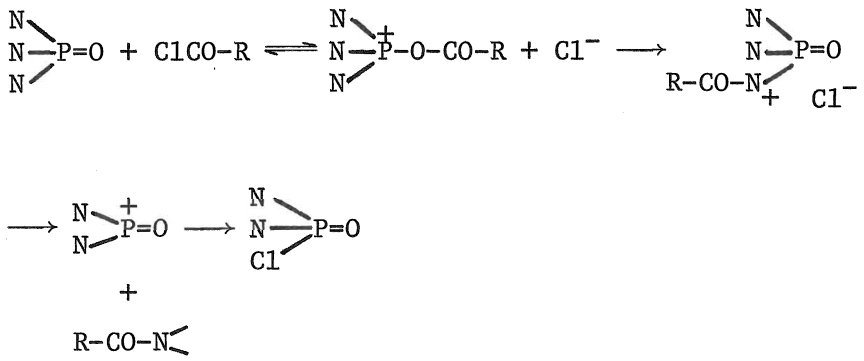
Although HMPA is quite stable to nucleophilic attack, a number of reactions with electrophiles have been observed in the past[43]. Carboxylic acids have been shown to give stable 1:1 complexes with HMPA, but transamidation occurs at 180-200°[46]. The reaction has been extended to aromatic, unsaturated and heterocyclic carboxylic acids as well as sulfonic acids[47]. In this work the acid and HMPA were present in a 3:1 ratio and the dimethylamide of the acid together with H_3PO_4 were produced. i.e.,



Attempts to apply this type of substitution to alcohols (both primary and secondary) resulted in dehydration to olefins as the main reaction[43]. However, benzyl alcohols were found to react with HMPA to give the corresponding benzyl dimethylamines after brief refluxing[49].

Although phenols give fairly stable 1:1 complexes of unknown structure with HMPA[43], no nucleophilic displacements have been reported.

Acyl chlorides are known to react easily with HMPA and on heating $N(CH_3)_2$ displaces Cl[43].



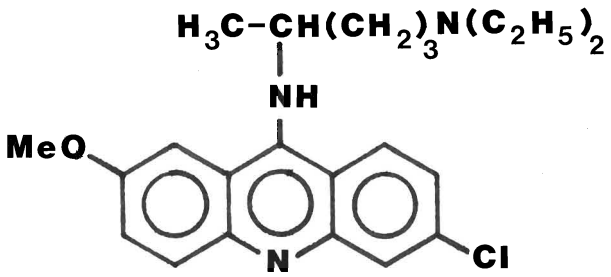
However, interestingly enough, it has been reported that HMPA is inert towards Cl → $N(CH_3)_2$ substitution in the aromatic compounds (e.g., p-NO_2-C_6H_4Cl)[50].

On the basis of previously reported information it was decided that the reaction of a series of suitably activated aryl halides and phenols with HMPA should be investigated. The possibility of reacting the chloroanthraquinones of main interest in this work with HMPA was also considered, since alternate syntheses (i.e., with Me_2NH or DMF) have seemed unsuitable in the past[22,23].

DISCUSSION

The reactions of some substituted anthraquinones with strong base

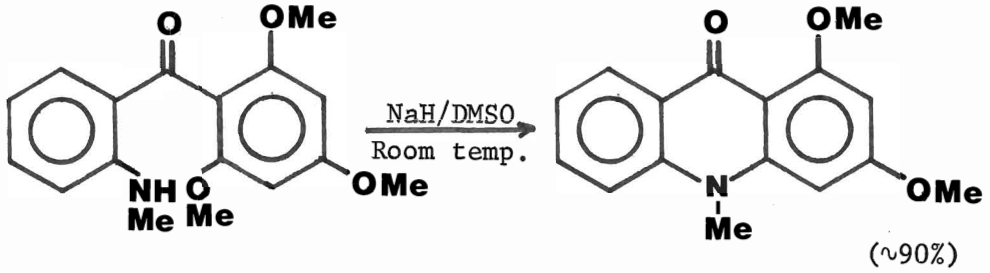
There has been considerable interest in acridine derivatives for some time, largely due to their valuable chemotherapeutic properties. For example, 6-chloro-9-(4-diethylamino-1-methylbutyl)amino-2-methoxyacridine (XXXVI), which is also known as "Atebrin", "Quinacrine" and "Mepacrin"[51], has been successfully used as an antimalarial agent since World War II. A substantial amount of work has been done on the bacteriostatic properties of numerous aminoacridines, especially 5-aminoacridines[52], and a number of diamino-acridine derivatives are used medically in treating sleeping sickness and amoebic dysentery.



XXXVI

Interest has also been shown in acridone derivatives, as precursors to various acridines and otherwise. Recently a number of acridone-carboxylic acid derivatives have reportedly shown anti-allergic activity[53].

In the past, acridones have been prepared by a high-temperature Ullmann condensation followed by high temperature treatment with acid or by utilizing a Chapmann rearrangement[54]. Although more recent work[55] has reported the low temperature preparation of the N-methylacridone (XXXVIII) from tecleanone (XXXVII), it was thought that a new acridone synthesis might be useful.

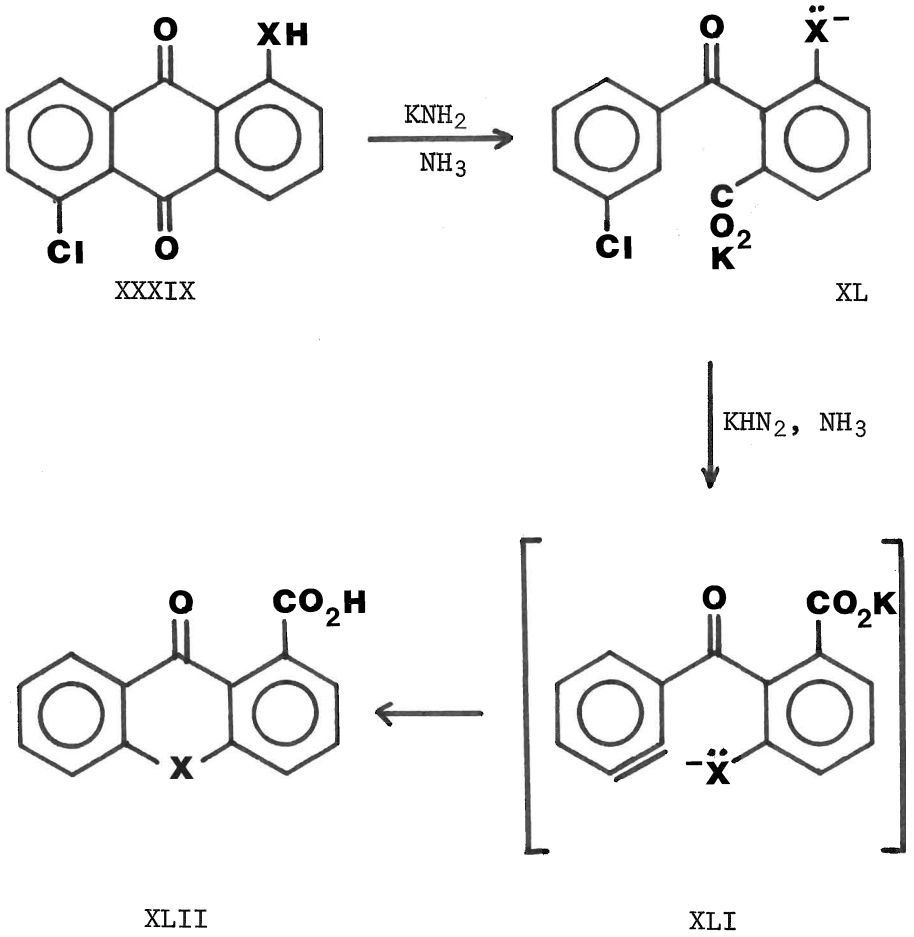


XXXVII XXXVIII

Kayser and Gibson[113] showed that 1,5-dichloroanthraquinone, when treated with potassium amide in liquid ammonia, gave 3-chlorobenzoic acid exclusively.

It was thought that replacement of one of the chlorines with a comparatively less electron-withdrawing group (X = RN-, -O-, -S-) would

allow for simple cleavage only at the carbonyl adjacent to the remaining chlorine to give a benzophenone derivative (XL). An aryne intermediate such as (XLI) could then be generated under these conditions. Intramolecular addition of the side-chain nucleophilic centre $-\ddot{X}^{-}$ should then be possible with subsequent addition of a proton to give (XLII).



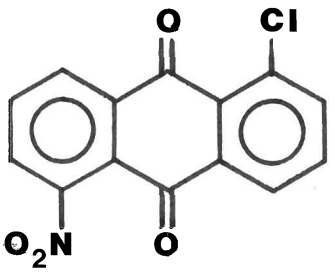
XXXIX XL

XLII XLI

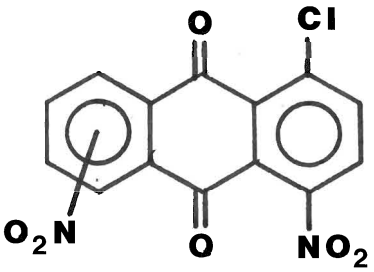
This objective was in fact realized in the case where X = -NMe[21] to give an acridone-1-carboxylic acid (N-methylacridone-1-carboxylic acid, obtained in 47% yield).

The initial purpose of this work was to find syntheses for the required starting material (XXXIX) where XH = $-NH_2$, -OH and -SH.

It was thought that an amino-group might well be introduced indirectly by first preparing a nitroanthraquinone and then reducing this to the appropriate amine with a suitable reagent (e.g., ammonium sulfide). Anthraquinone is known to give far more 1-nitro than 2-nitro-anthraquinone under nitrating conditions[56]. This is consistent with the predominance of ortho-nitration over para-nitration observed in simpler carbonyl compounds[57]. Thus, 1-chloroanthraquinone was nitrated with a sulfuric acid-nitric acid mixture in the hope that 1-chloro-5-nitroanthraquinone (XLIII) would be produced. However, mass spectral evidence suggested that two nitro-groups had in fact been introduced. Since it was found that previous attempts to nitrate 1-chloroanthraquinone[58] gave what was identified as 1-chloro-4-nitroanthraquinone, the new compound was identified as 1-chloro-4,X-dinitroanthraquinone (XLIV) (where X = 5 or 8).



XLIII



XLIV

It was obtained in good yield (60%) but was not used in a further attempt to prepare an amino-anthraquinone. Very recent work[59] has however reported the synthesis of acridones in good yield by the ring closure of suitably substituted nitro-benzophenones. Study of the reactions of nitro-anthraquinones with strong base may be in order.

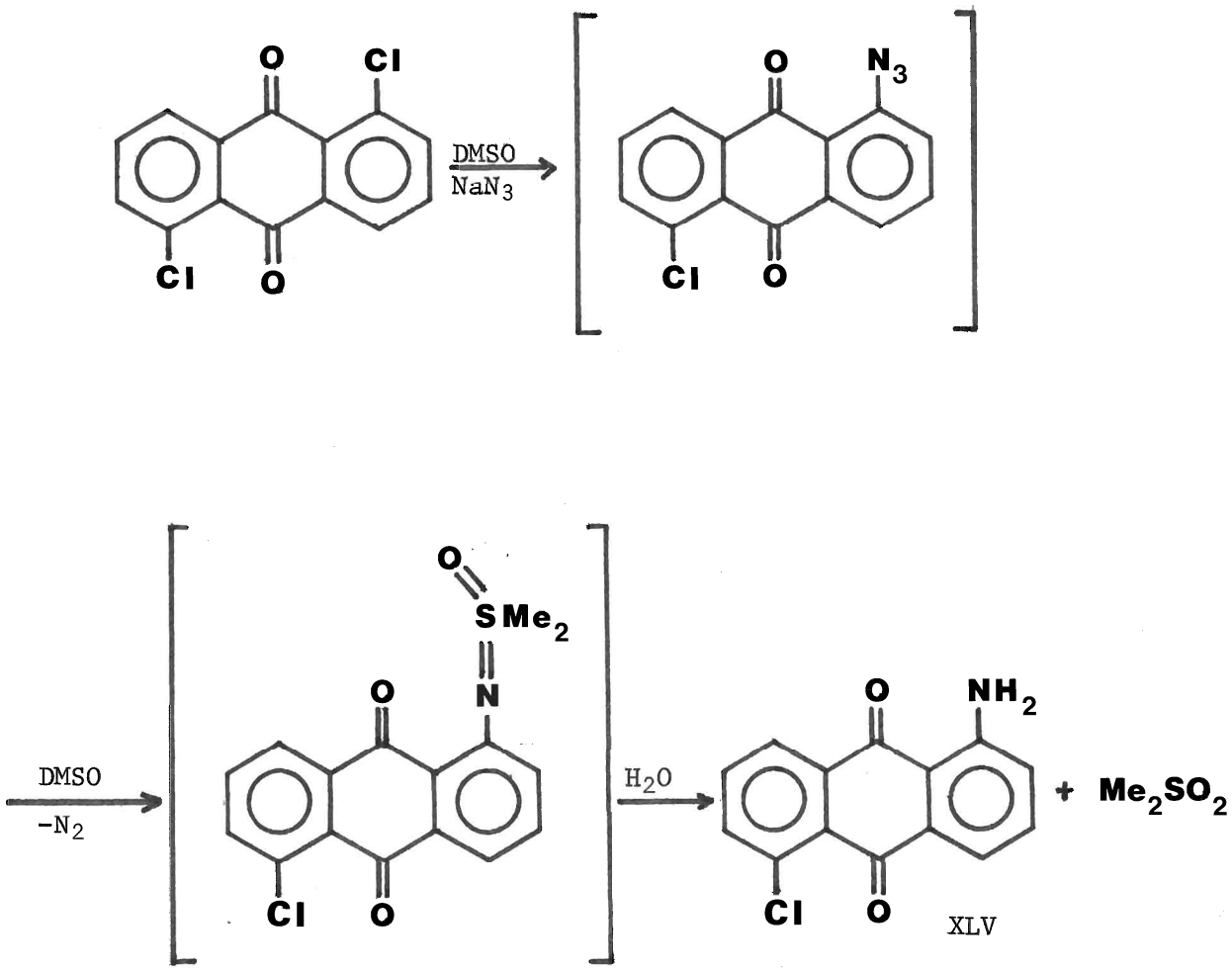
Since other reactions using p-toluenesulfonamide and formamide[21] were unsuccessful in converting chloroanthraquinones to aminoanthraquinones, an alternate method for introducing an $-NH_2$ group to an anthraquinone skeleton was required. It was thought that a reaction analogous to that of 2-chloro-1,4-naphthaquinone[2] and sodium azide in ethanol might be developed for chloroanthraquinones.

However, due to lack of solubility, 1,5-dichloroanthraquinone did not react with sodium azide in refluxing ethanol even after ten hours. Nor was any reaction observed in acetonitrile or acetic acid. Clearly, a solvent was required which was at least higher boiling than those already used. It was found that 1,5-dichloroanthraquinone reacted readily with sodium azide in dimethylsulfoxide (DMSO) after 30 minutes to give 1-amino-5-chloroanthraquinone (XLV) in reasonable yield (33%). The reaction was, however, complicated by the fair amount of intractable material produced and the fact that the desired product could be separated from side-products and unreacted starting material only by the use of a long chromatographic column.

Relatively small, non-polarizable ions such as N_3^- are known to be quite sensitive to solvent change in bimolecular aromatic nucleophilic substitution reactions and polar aprotic solvents (e.g., DMSO) are known to enhance reaction rates in these cases[69].

Although a reduction of an azide substituent to an amino group must have occurred, a mechanism is not immediately obvious. An intramolecular redox reaction of the type presumed in the reaction of 1,4-naphthaquinone[2] and thymoquinone[3] with hydrazoic acid is not likely. However, the possibility of a reaction involving the capture of a nitrene by DMSO is not unprecedented[70].

This could be rationalized in terms of the following scheme.



In an attempt to improve the yield of (XLV) an alternate synthesis was explored. This involved the direct reaction of 1,5-dichloro-anthraquinone with ammonia (gas) in DMSO (~100°) in the presence of potassium fluoride. The reaction was enhanced by the addition of potassium fluoride which is reported to participate in strong hydrogen bonding[60,61] providing a good source of anions. Since the solvent (DMSO) is polar and aprotic, F^- is not solvated appreciably and ammonia can act as a hydrogen donor (for hydrogen bonding) and the nucleophilicity of the nitrogen is increased so as to facilitate substitution.

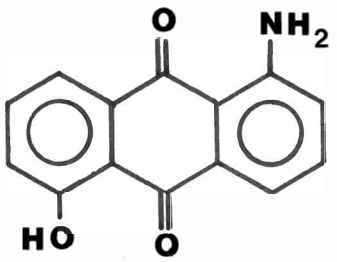
Although the yield in this reaction is not substantially greater than that of the previous reaction, it offers an alternate route to the preparation of aminoanthraquinones from chloroanthraquinones.

Once the amino-anthraquinone (XLV) had been successfully prepared it was reacted with potassium amide in liquid ammonia in an attempt to produce acridone-1-carboxylic acid via a benzyne intermediate. However, even after a five hour reaction time, none of the desired product was observed. Instead, the starting material was recovered (60%). It is interesting to note that 2-amino-2'- and -3'-chlorobenzophenone were also recovered (91 and 78%, respectively) from similar treatment[19]. However, simple benzoylation of these amines and subsequent reaction with potassium amide in liquid ammonia afforded N-benzoylacridone (67 and 36%, respectively)[19]. Acetamido-benzophenones have also been reported to cyclize more readily to give substituted acridones than the analogous aminobenzophenones[55].

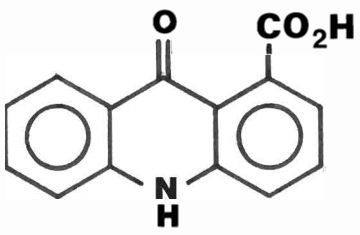
Investigation of the reaction of 1-benzamido- and/or 1-acetamido-5-chloroanthraquinone with potassium amide in liquid ammonia seems to

be in order. Both these compounds are readily accessible from the starting material (XLV).

Although 2-amino-2'- and -3'-chlorobenzophenone were recovered when treated as above, conversion to acridone was successfully achieved by the action of potassium t-butoxide in refluxing t-butylbenzene[62]. Treatment of (XLV) with excess potassium t-butoxide in refluxing t-butylbenzene for twelve hours mainly returned the starting material (67%). However, a small amount (3%) of bicarbonate-soluble material was obtained and this was identified as 1-amino-5-hydroxyanthraquinone (XLVI) rather than acridone-1-carboxylic acid (XLVII).



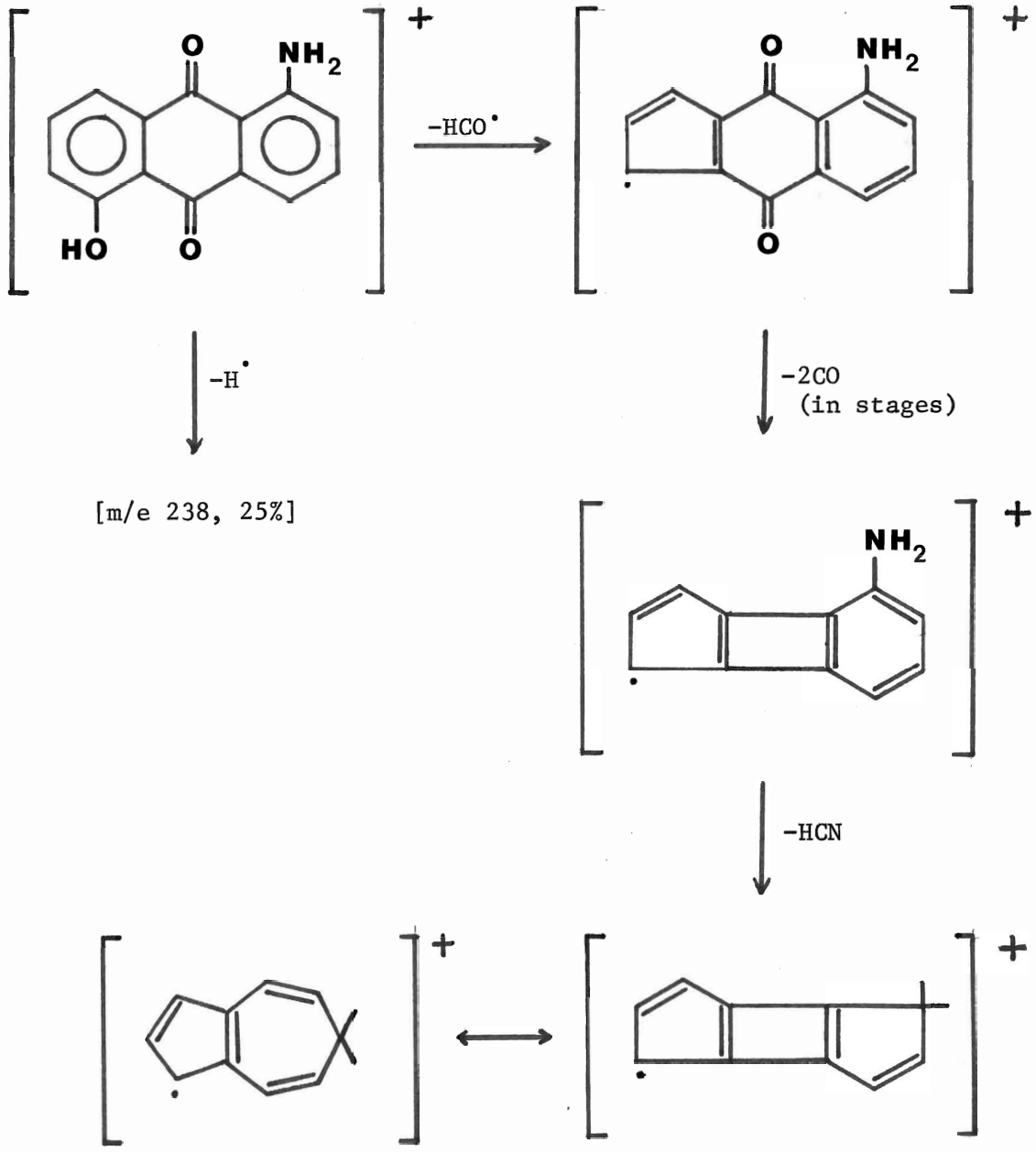
XLVI



XLVII

Since the sample could not be obtained analytically pure, identification was made mainly on the basis of the mass spectral evidence. Besides showing a strong molecular ion peak, the mass spectra of anthraquinones characteristically show fragments corresponding to the loss of one and two CO molecules, and in hydroxyanthraquinones loss of -HCO is also observed. The fragmentation observed for (XLVI) can be rationalized as per Scheme 2.

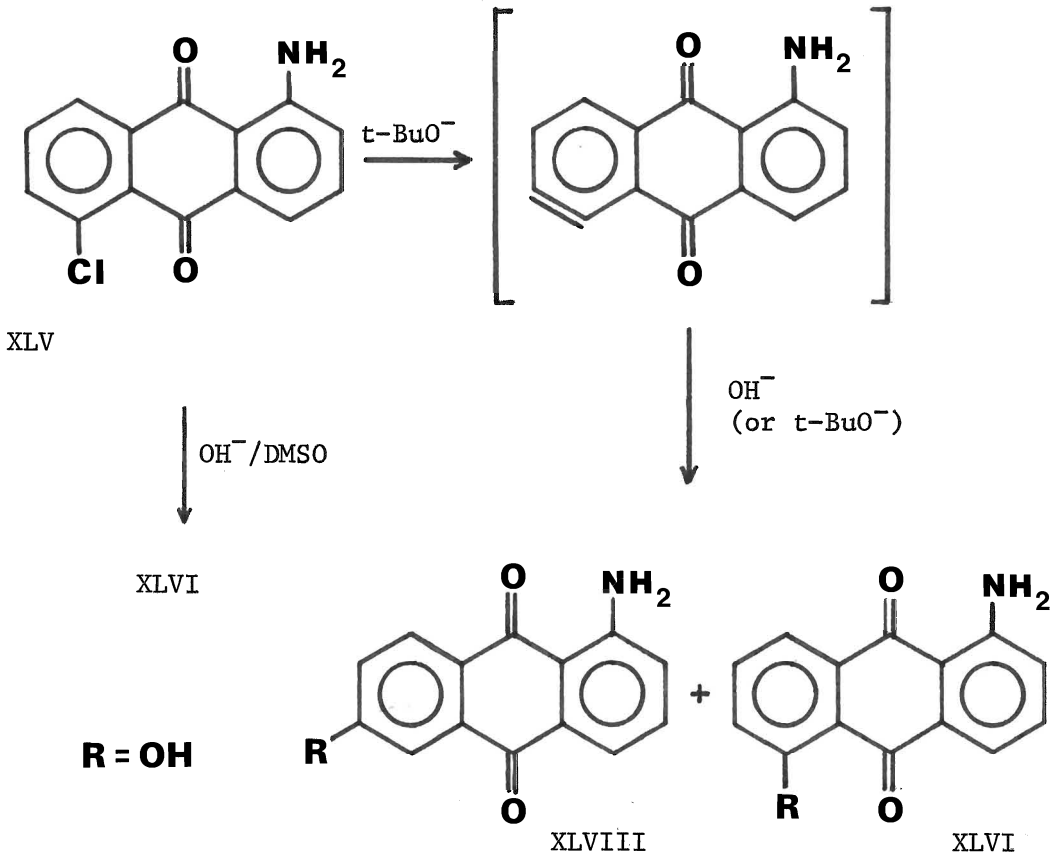
SCHEME 2



The identification was confirmed by comparison with the mass spectrum of a sample of (XLVI) prepared by treating (XLV) with potassium hydroxide in DMSO for one hour.

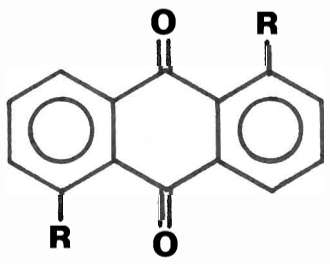
This seems to indicate that (XLVI) was produced by a simple nucleophilic substitution rather than via an aryne intermediate which should also give 1-amino-6-hydroxyanthraquinone (XLVIII).

i.e.,

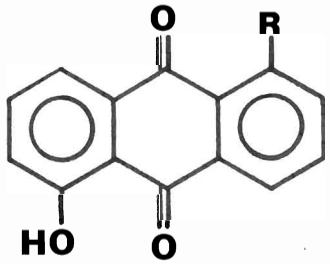


It is not clear why no cleavage or rearrangement products were observed and further work with N-substituted amino-anthraquinones might resolve this problem.

A number of procedures were tried in an attempt to prepare the hydroxy-analogue of (XLV). Again, difficulties were encountered in the choice of solvent. An initial attempt involved treating 1,5-dichloroanthraquinone with potassium hydroxide in refluxing 2-ethoxyethanol (cellosolve). Two products were isolated, however neither was the desired one. Instead it appeared that the solvent had become involved in nucleophilic substitution to give 1,5-di(2-ethoxy-ethoxy) anthraquinone (XLIX) and 1-(2-ethoxy-ethoxy)5-hydroxyanthraquinone (L). This was not expected since previous reactions of halogeno-benzophenones in the presence of potassium carbonate in refluxing 2-ethoxyethanol did not produce any 2-ethoxyethyl ethers[63].



XLIX



L

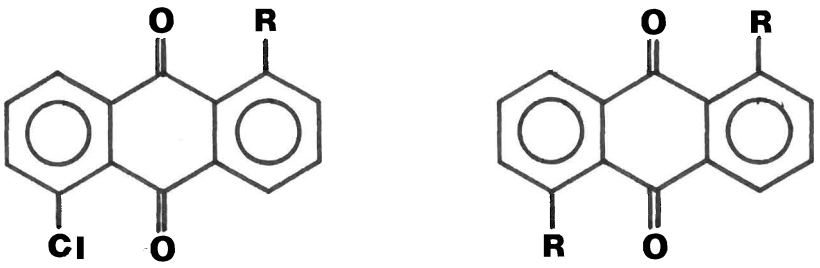
R = $-OCH_2CH_2OCH_2CH_3$

These structures were confirmed by mass spectral fragmentation and by the n.m.r. spectra. The latter showed the presence of two coupled methylenes and an ethyl spin system together with an aromatic multiplet.

The reaction proceeded easily, yields were fairly good and separation and purification were relatively easy. This type of reaction may have some use in the preparation of various long-chain

alkyl ethers of anthraquinones. However, these compounds were not suitable for the type of work undertaken here.

It has been reported[64] that o- and p-nitro-chlorobenzenes give the appropriate phenols when treated with sodium hydroxide in DMSO. Pentachlorophenol has also been prepared in 97% yield[65] by reacting hexachlorobenzene with sodium hydroxide in DMSO at 100-110°. This led to the attempt to produce 1-hydroxy-5-chloroanthraquinone (LI) from 1,5-dichloroanthraquinone under similar conditions. This route seemed quite promising when an initial reaction showed no starting material returned (t.l.c.). However, unfortunately, mass spectral evidence showed the product to be a mixture of (LI) and what is thought to be 1,5-dihydroxyanthraquinone (anthrarufin) (LII), with some starting material also present.

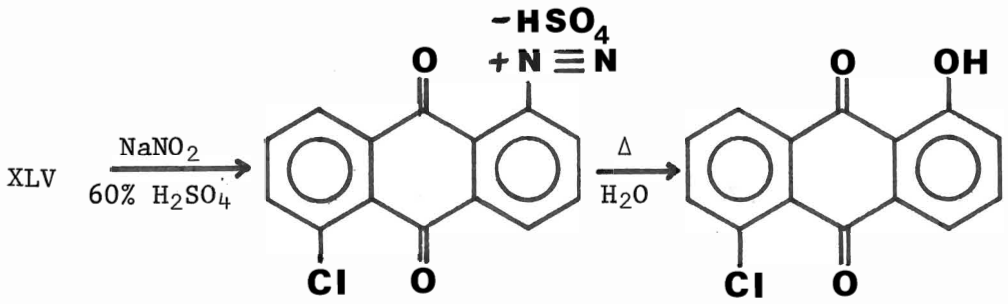


LI **R= OH** LII

Although the hydroxyanthraquinones could be separated from the starting material they could not be effectively separated from each other by chromatography. Mass spectral monitoring of the reaction showed that both compounds were produced in appreciable quantities even after only fifteen minutes. This problem could also not be overcome by using only an equimolar quantity of potassium hydroxide and 1,5-dichloroanthra-

quinone. Hence, this procedure was abandoned.

Eventually (LI) was prepared by a literature method[66] involving the diazotization of (XLV) and subsequent decomposition of the diazonium salt (LIII).



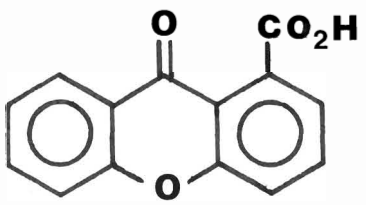
LIII LI (19%)

The reaction was done in sulfuric rather than hydrochloric acid because (1) salt formation was easier in sulfuric acid and (2) use of hydrochloric acid would produce some 1,5-dichloroanthraquinone during decomposition of the diazonium salt.

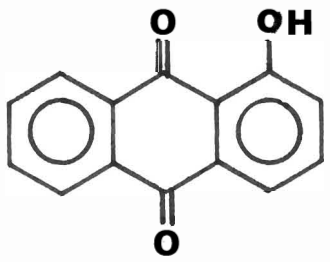
Having prepared the requisite starting material (LI) an attempt was made to obtain xanthone-1-carboxylic acid (LIV) under the conditions used previously in the attempt to prepare (XLVII). A previous synthesis of (LIV)[67] involved a four-step procedure which required the cyclization of a carboxy-cyanodiphenyl ether with phosphoryl chloride and subsequent basic hydrolysis. This method gave (LIV) in 8% overall yield. Investigation of an alternate route seemed in order.

Treatment of (LI) with potassium amide in liquid ammonia gave almost quantitative recovery (91%) of the starting material. It is not obvious why no reaction was observed since a series of hydroxy-chlorobenzophenones have been previously cyclized to substituted xanthones under similar conditions[20].

Treatment of (LI) with potassium t-butoxide in refluxing t-butylbenzene for twelve hours gave more surprising results. The base insoluble fraction was chromatographed to give a small amount of the starting material (2%) but a substantial amount of red material remained strongly adsorbed to the silica gel and was not identified. Chromatography of the base-soluble fraction gave a small amount (5%) of what was identified as 1-hydroxyanthraquinone (LV). The structure was confirmed by comparison with an authentic reagent sample.



LIV

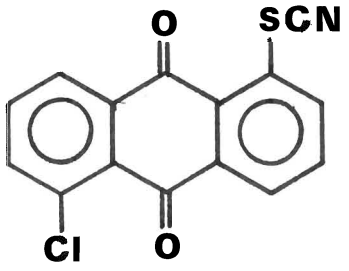


LV

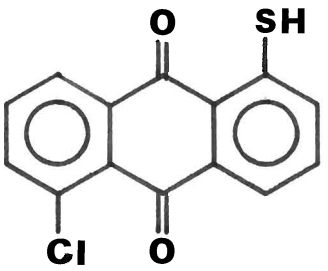
The origin and mechanism of formation of (LV) is not at all clear. Although it may have originated from an impurity in the starting material, it seems doubtful that the sample of (LI) used contained at least 5% of one impurity. Mass spectral data did not indicate any major impurities in any of the precursors in the three steps leading to the formation of (LV). This result remained unexplained.

Attempts to prepare the sulfur analogue of (LI) were basically unsuccessful. One attempt involved the diazotization of (XLV) and subsequent reaction with sodium sulfhydrate ($NaSH \cdot xH_2O$). The starting material was in the most part (60%) recovered and a small amount of a mixture containing sulfur (S_8) and an unidentified component (m/e 254) was also obtained. None of the desired compound was observed.

Reaction of 1,5-dichloroanthraquinone with potassium thiocyanate in DMSO was attempted in an effort to introduce sulfur functionality. Although the mass spectrum of the reaction mixture showed a small peak at m/e 299 (which corresponds to structure (LVI)), it contained mainly starting material and not enough of the thiocyanate was produced for further experimentation.



LVI

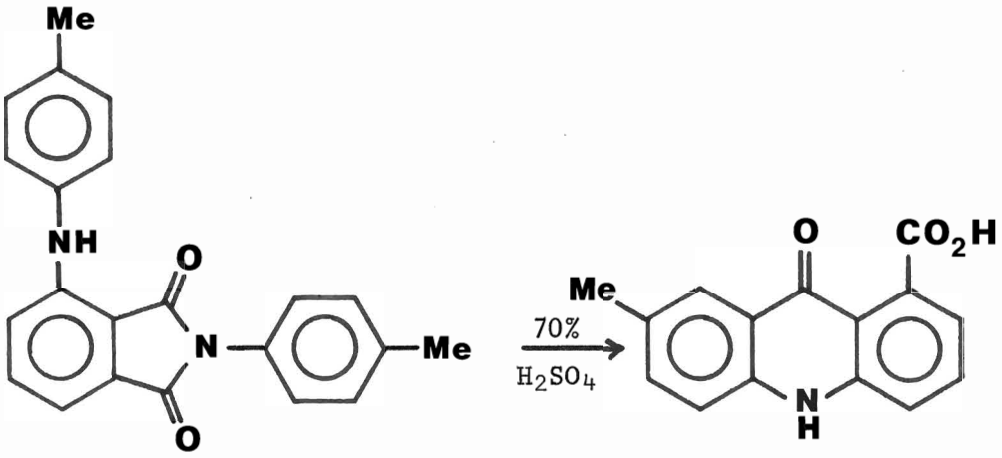


LVII

One possible route to (LVII) which could not be investigated was via 5-chloro-anthraquinone-1-sulfonic acid (LVIII), which has been prepared from anthraquinone-1,5-disulfonic acid in the presence of hydrochloric acid and sodium (or potassium) chlorate[68]. Reduction of (LVIII) by a suitable method (e.g., sodium hydrosulfite) should yield (LVII).

Attempted preparation of an acridone from an anthraquinone under acidic conditions

While working with a series of arylaminophthalic acid derivatives Marriott and Robinson[71] were able to prepared 7-methylacridone-1-carboxylic acid (LIX) by dehydrating 3-p-toluidino-N-p-tolyl-phthalimide (LX) in 70% sulfuric acid.

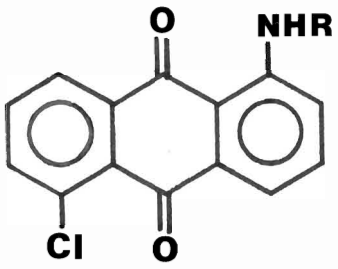


LX LIX

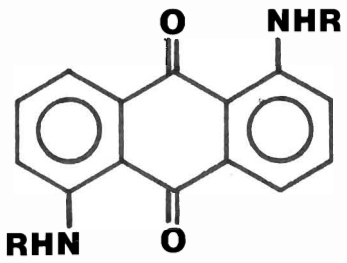
It was thought that an analogous type of reaction might be possible in the anthraquinone series if suitable starting materials could be prepared.

In order to prepare 1-p-toluidino-5-chloroanthraquinone (LXI), 1,5-dichloroanthraquinone was refluxed with p-toluidine for fifteen minutes. The copper catalyst, cupric acetate and potassium carbonate used in similar condensations[25,26] were not employed here because the reaction was found to be at least as efficient without

them. After chromatographing twice, (LXI) was isolated as dark red needles (37%). 1,5-Bis(p-toluidino)anthraquinone (LXII) (as well as some other minor products) was also obtained as black needles with a golden reflex (5%).



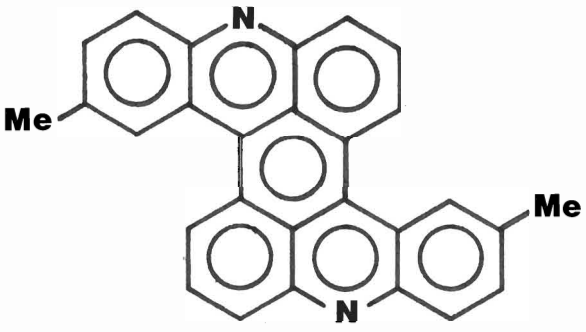
LXI



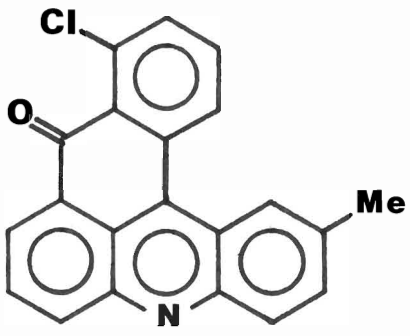
LXII

R = $-C_6H_4CH_3$

Reaction of (LXII) in 70% sulfuric acid gave a dehydration reaction to yield the diacridine (LXIII). Under the same conditions (LXI) gave the acridine (LXIV)(58%).



LXIII

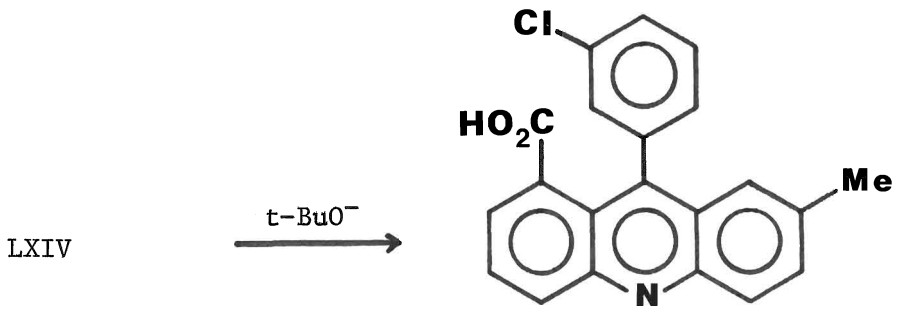


LXIV

Dehydration of this type is probably favoured because of the aromatocity which is achieved. The mechanism for the formation of (LXIV) can be summarized as follows (Scheme 3).

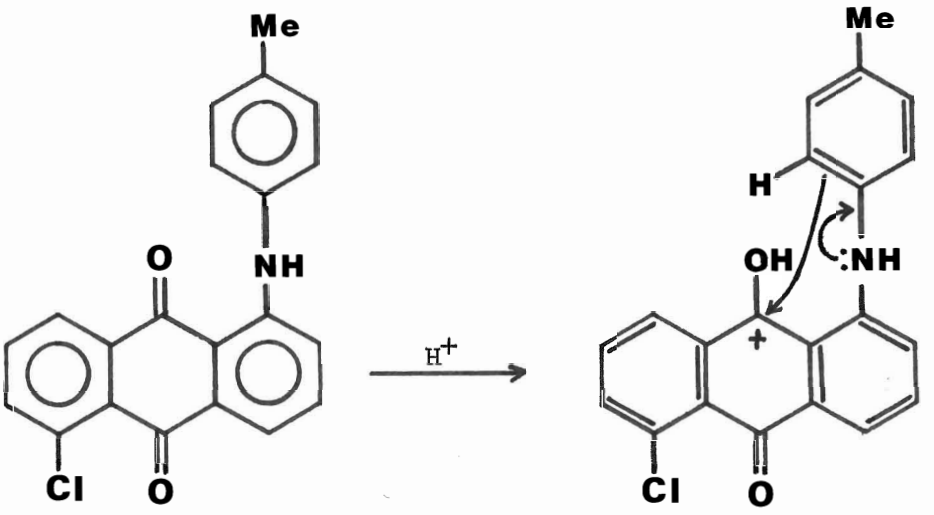
Although (LXIII) is a very stable molecule (as seen by high m.p. and high incidence of doubly charged ions in the mass spectrum) and not highly functionalized, (LXIV) has retained some functionality and could undergo further reactions.

It was thought that cleavage at the carbonyl might be effected using the potassium t-butoxide-water reagent which was used previously to cleave substituted benzophenones[28] and anthraquinones[31]. If analogous cleavage occurred it was hoped that it would be specific (as previously[28]) to give mainly the acridine-carboxylic acid (LXV).

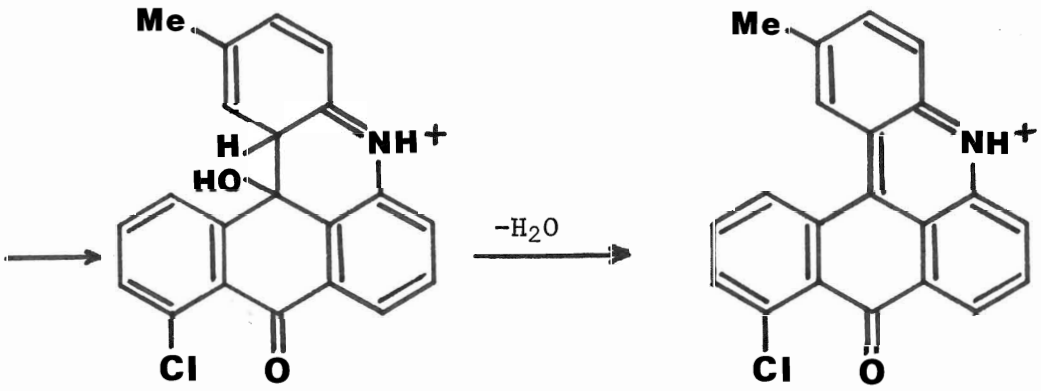


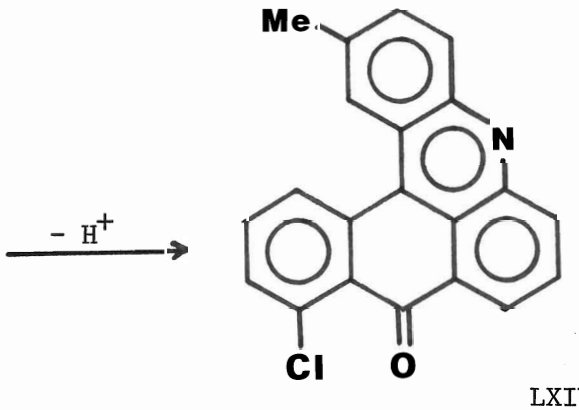
LXV

However, unfortunately the reaction gave a complex mixture and there was no evidence for the presence of (LXV). Less severe conditions such as a lower reaction temperature and/or the use of less basic reagents (e.g., potassium hydroxide) might make (LXV) accessible; however time did not allow for further study of this type of reaction.



LXI

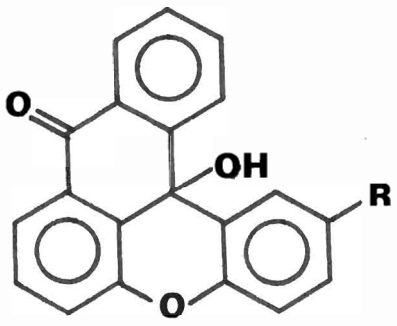




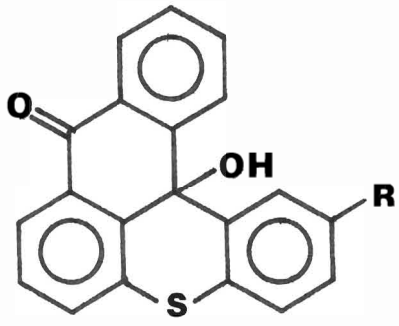
LXIV

SCHEME 3. Mechanism for the dehydration of 1-p-toluidino-5-chloroanthraquinone.

Similar compounds have been prepared where oxygen[72] and sulfur[73] are the hetero-atoms, by the dehydration of phenoxy- and thiophenoxy-anthraquinones. It would be interesting to examine the possible reactions of compounds like (LXVI) and (LXVII) to produce substituted xanthones and thioxanthones.



LXVI

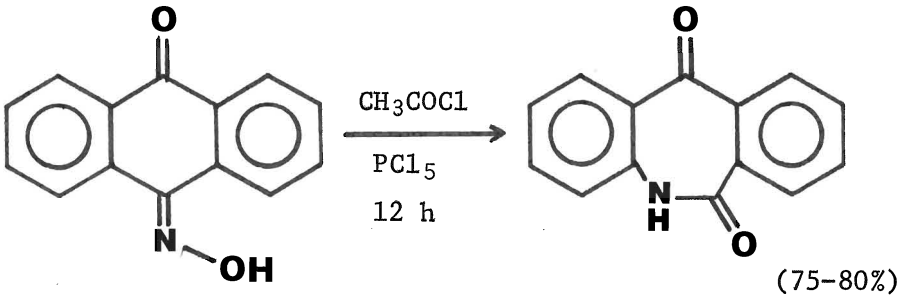


LXVII

R = Me, H

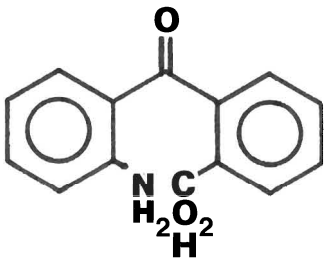
The reaction of various anthraquinones with sodium azide

The azepindione (LXVIII) was first prepared by Beckmann[74] in 1923 via rearrangement of the anthraquinone-oxime (LXIX).



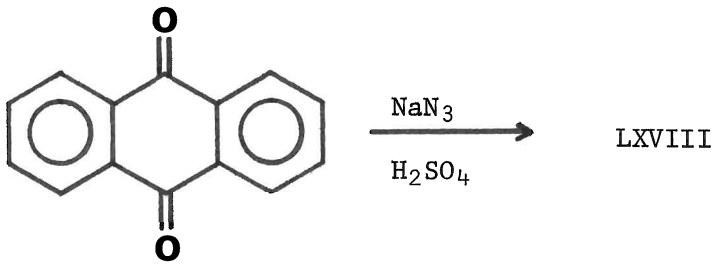
LXIX LXVIII

The azepindione (XV) was found to be readily hydrolyzed in aqueous sodium hydroxide to give the acid (LXX). This compound could not be recyclized even at 160° in concentrated hydrochloric acid.



LXX

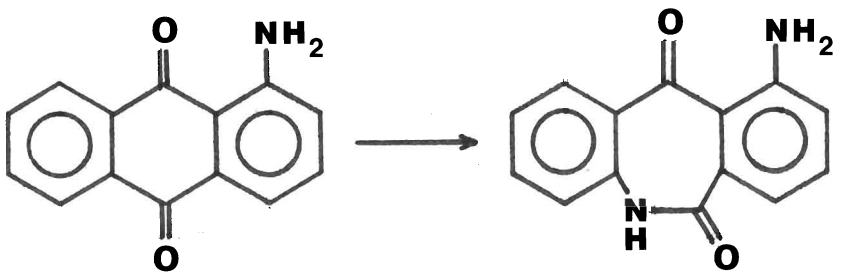
Later, in work involving the reactions of hydrazoic acid in sulfuric acid, Caronna[75] obtained the same compound by the reaction of sodium azide in sulfuric acid with anthraquinone (LXXI), although no yield was given.



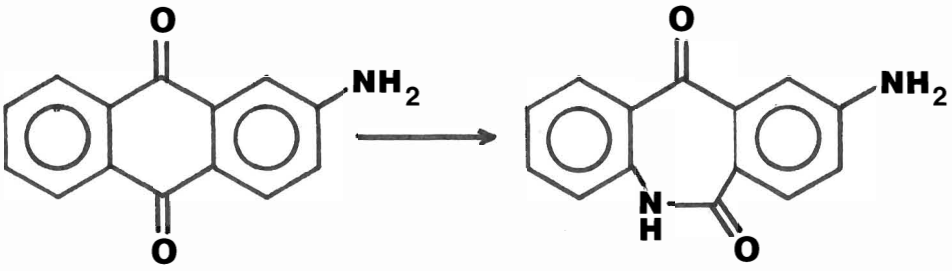
LXXI

In the present work, it has been shown that anthraquinone, under essentially Schmidt conditions (done before finding Caronna's previous work) gave results consistent with those obtained previously[75].

It was further shown by Caronna that both 1- and 2-aminoanthraquinone reacted with sodium azide in sulfuric acid after 12 hours to give the azepindiones (LXXII) and (LXXIII), respectively.

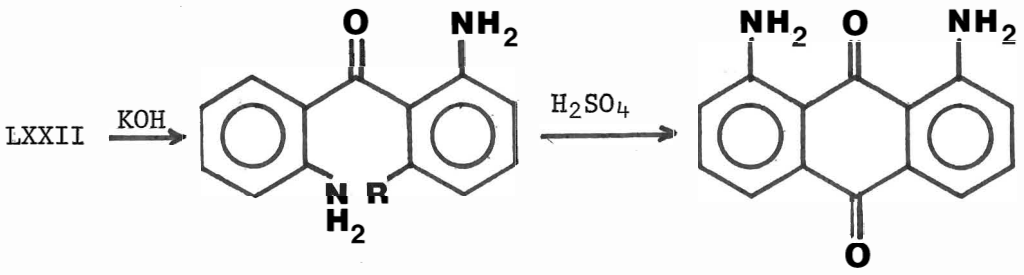


LXXII



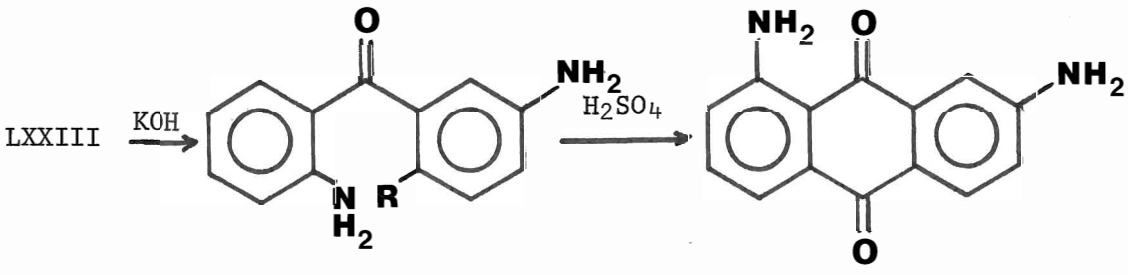
LXXIII

Heating of these compounds in aqueous potassium hydroxide gave the appropriate amino-acids (LXXIV) and (LXXV). These were cyclized with concentrated sulfuric acid to give diaminoanthraquinones (LXXVI) and (LXXVII), respectively.



LXXII KOH H_2SO_4

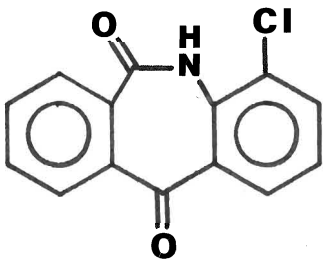
LXXIV LXXVI



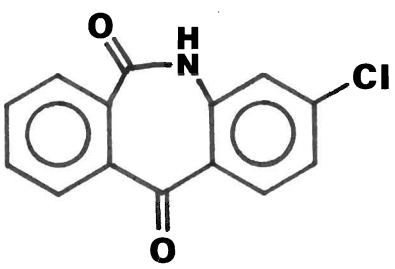
LXXIII KOH H_2SO_4

LXXV $R = CO_2H$ LXXVII

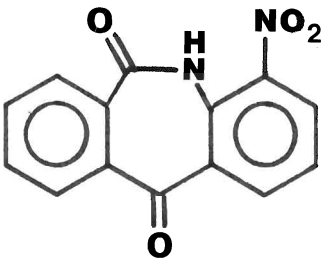
In contrast with aminoanthraquinones which insert -NH at the farthest possible site from the substituent, chloro- and nitro-anthraquinones were found to activate the nearest carbonyl and introduce -NH adjacent to the substituent[76]. Thus, 1- and 2-chloroanthraquinones and 1-nitroanthraquinone reacted (24 hour reaction times) to give the azepindiones (LXXVIII-LXXX) respectively.



LXXVIII



LXXIX



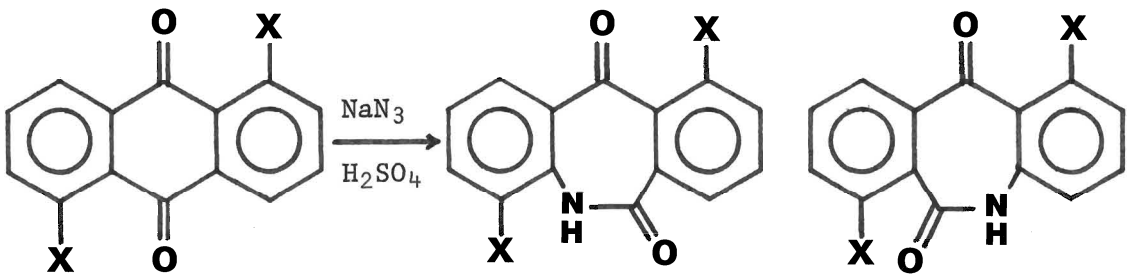
LXXX

These compounds were readily cleaved by aqueous potassium hydroxide to give the appropriate amino-acids, which in the case of (LXXVIII) and (LXXIX) gave aminoanthraquinones on heating in concentrated sulfuric acid, and recyclized to the azepindione in the case of (LXXX).

The present work is concerned with the reaction of several chloroanthraquinones with sodium azide in sulfuric acid. All the reactions proceeded readily and in good yields under the conditions used, but isomeric mixtures were found in all cases. Previous work claiming the selective production of single isomers in this type of reaction[35,36] has been brought into question by workers who obtained mixtures[37,38] in proportions which are consistent with the mechanistic

considerations involved. The single isomers (LXXVIII) and (LXXIX) reported by Caronna were only found in admixture with at least one other isomer during the present work.

Work in this vein was initiated by reacting 1,5-dichloroanthraquinone with sodium azide in sulfuric acid. The reaction gave a mixture of two isomers (as indicated by t.l.c. and mass spectrum) in good yield. The mass spectrum is consistent with structures (LXXXI) and (LXXXII).



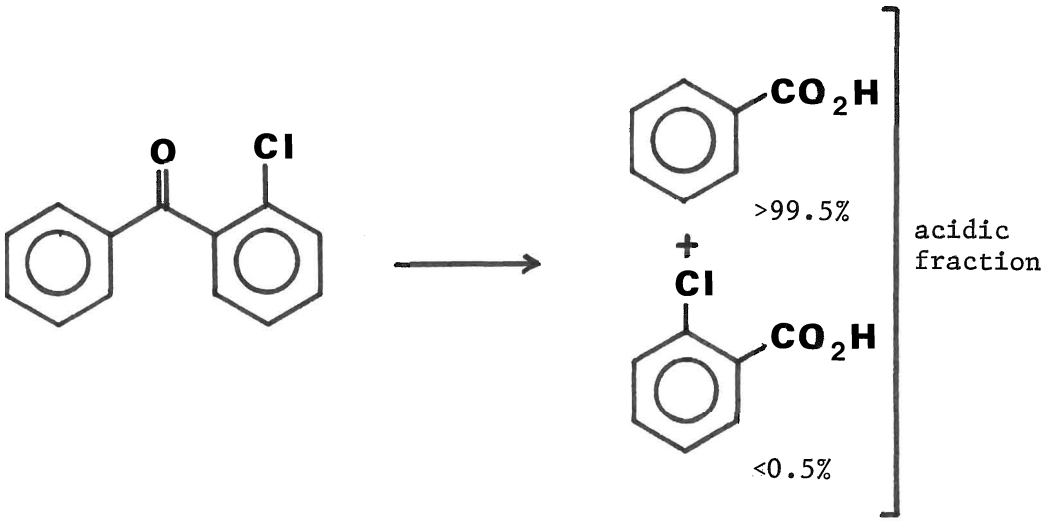
X= Cl LXXXI LXXII

Due to poor solubility in most organic solvents and the similarity of R_f values, these compounds could not be separated by conventional chromatographic techniques. An alternate method for separation and identification was thus required.

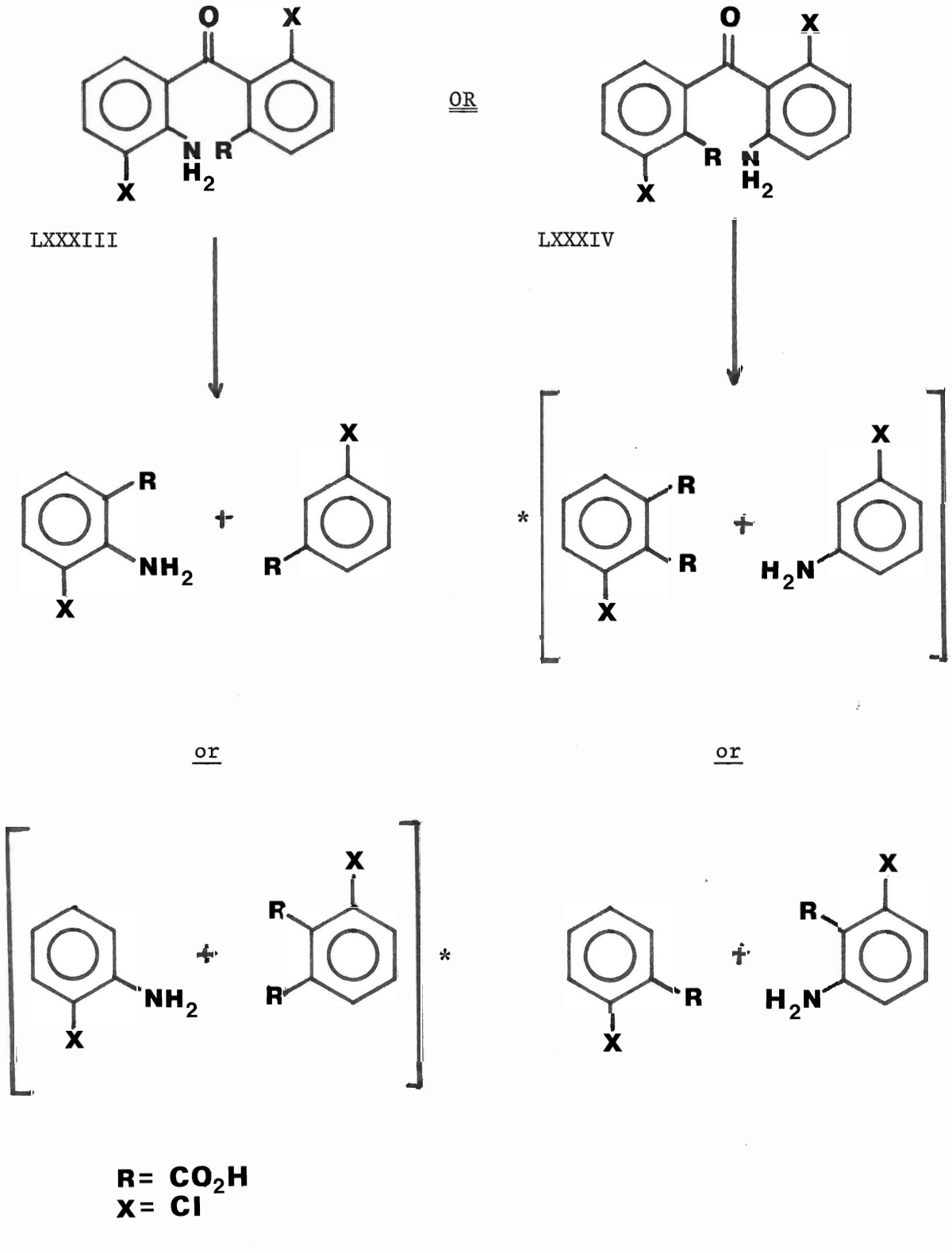
These compounds are known to be fairly readily hydrolyzed by dilute potassium hydroxide solution. It was found that brief heating of the mixture in dilute ethanolic potassium hydroxide (approximately 2% w/v) resulted in preferential hydrolysis of one of the isomers (monitored by t.l.c.) to give an amino-acid which easily separated from the

unaffected isomer. T.l.c. showed that the more mobile isomer was hydrolyzed and that the isomer of lower R_f remained intact. Inspection of structures (LXXXI) and (LXXXII) suggested to this worker that the former would be expected to have a higher R_f value than the latter. The lactam carbonyl of the former would also seem more sterically accessible to base-catalyzed hydrolysis than in the latter case.

Separation had thus been accomplished and tentative identification of the isomers had been made. However, more substantial identification was thought to be in order. Using the method for cleavage of benzophenones mentioned previously[28,29], the amino-acid was cleaved to give a mixture of benzoic acids. Since the cleavage of o-chlorobenzophenones (and o-carboxybenzophenones) was previously found[28] to occur mainly on that side of the carbonyl group which is closer to the substituent, e.g.,



the possible cleavage products can be summarized as in Scheme 4.

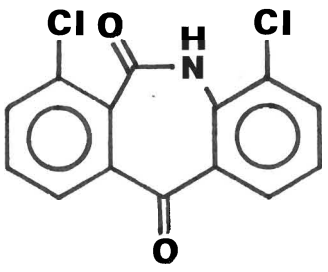


R= CO_2H
X= Cl

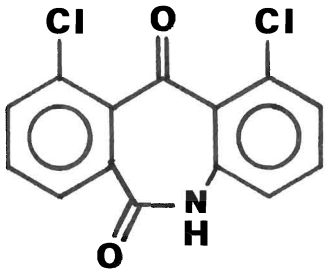
SCHEME 4: Basic Cleavage of Substituted Benzophenones (*not observed by mass spectrum.)

Identification of the amino-acid as (LXXXIII) or (LXXXIV) could then be accomplished by analysis of the cleavage products to check for the presence of o- or m-chlorobenzoic acid; this could be done by conversion to the methyl esters, followed by g.l.c. analysis. Comparison with known samples (unambiguously prepared) of methyl o- and m-chlorobenzoates showed only the presence of the m-compound, confirming the presence of m-chlorobenzoic acid in the cleavage mixture. Thus, azepindione (LXXXI) was preferentially hydrolyzed to give (LXXXIII) and the unaffected isomer was identified as (LXXXII). This substantiates the tentative identifications.

The reaction of 1,8-dichloroanthraquinone under Schmidt conditions also gave a mixture of two isomers in good yield. Only two possible structures exist (LXXXV and LXXXVI).

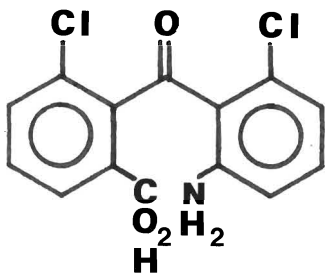


LXXXV



LXXXVI

Preferential hydrolysis returned one azepindione (after crystallization) as off-white prisms, considered to be (LXXXV) by analogy with the previous experiment, and an acid which is presumed to be (LXXXVII).

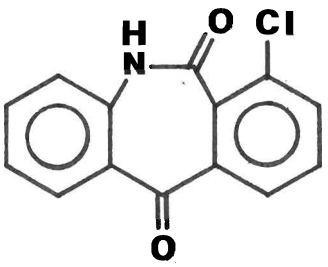


LXXXVII

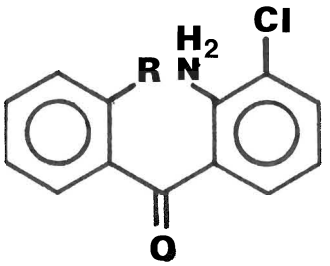
This acid was obtained as a dark yellow oil which could be crystallized (as bright yellow crystals) only after repeated attempts from ethanol/water. Calculations based on the presumed amounts of the cyclic products obtained suggest that (LXXXV) and (LXXXVI) were present in approximately 1:3 ratio.

From the work done previously by Caronna[76] using 1- and 2-chloroanthraquinone, it was concluded that a chlorine substituent activates the nearer carbonyl function and only gives the product from insertion of -NH on the side of the carbonyl group nearer to the substituent. These experiments were repeated in this work and found to give mixtures of insertion products in both cases.

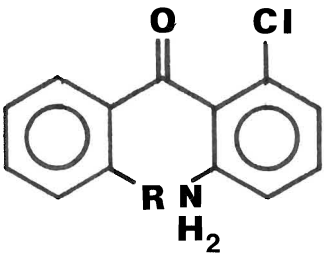
In the case of 1-chloroanthraquinone, the product of the reaction was found to be a two-component mixture which could be separated into a cyclic compound and an amino-acid by mild basic hydrolysis. By analogy with the two previous experiments the cyclic product which resisted hydrolysis was identified as (LXXXVIII). The amino-acid, however, could have three possible structures (LXXXIX-XCI).



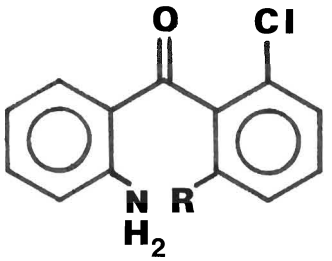
LXXXVIII



LXXXIX



XC



XCI

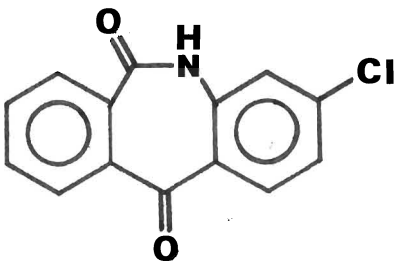
$R = CO_2H$

Assuming that Caronna's identification of his product (LXXVIII) was correct, one would favour structure (LXXXIX). However, the data obtained in this work are not sufficient to assure that the proposed structure is correct.

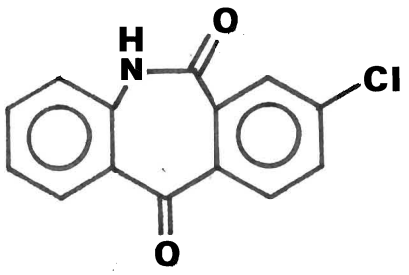
Compound (LXXXVIII) and what was tentatively identified as (LXXVIII) were obtained in approximately equal proportion with, perhaps, only a slightly greater amount of the latter being produced.

Similarly, 2-chloroanthraquinone gave two compounds (in comparable proportion) with practically identical R_f values which were both readily hydrolyzed under mildly basic conditions to give an inseparable

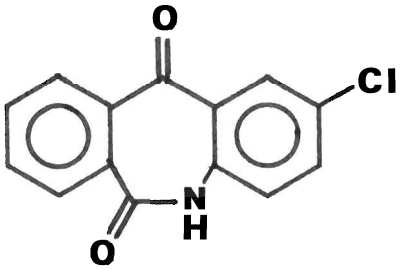
mixture of acids. This case is more complex than the previous ones since, in principle, four possible isomers exist (LXXIX, XCII-XCIV).



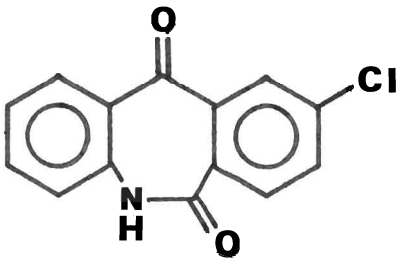
LXXIX



XCII

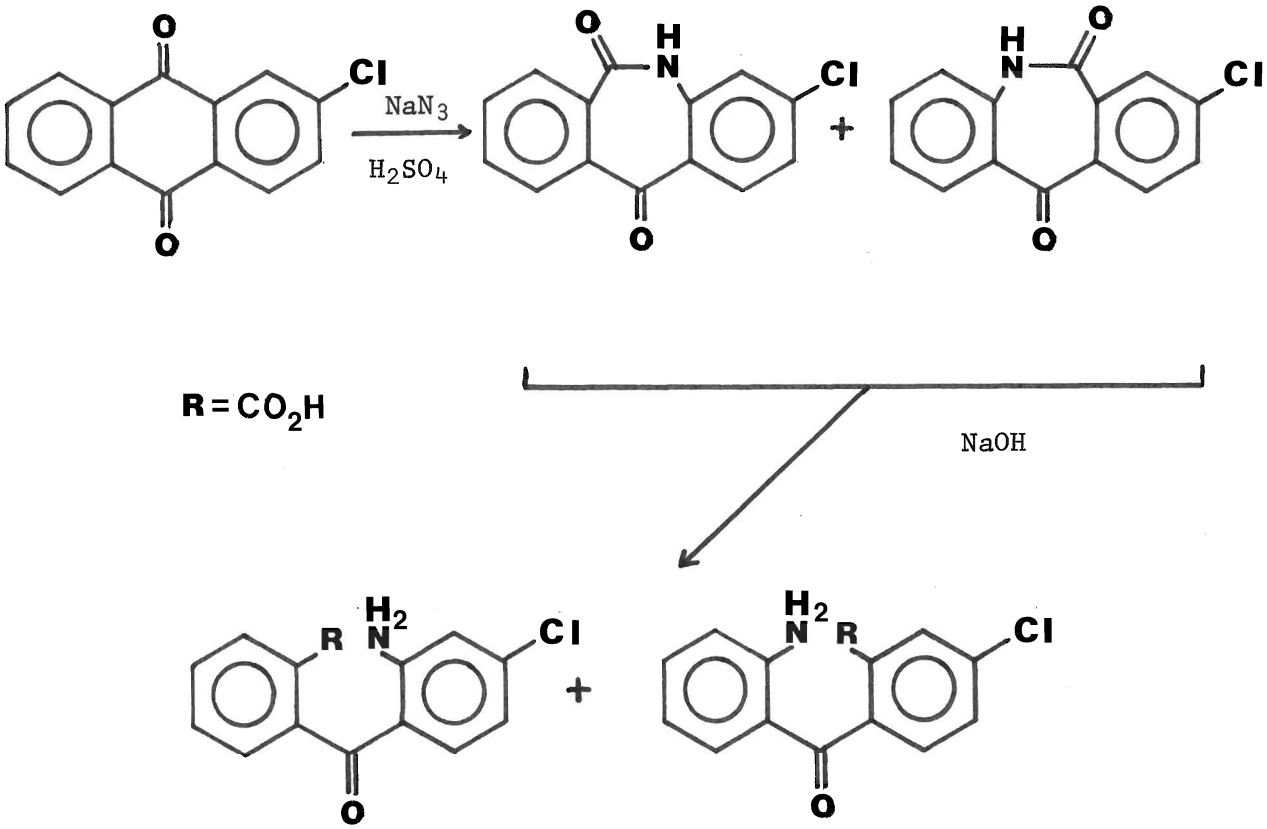


XCIII

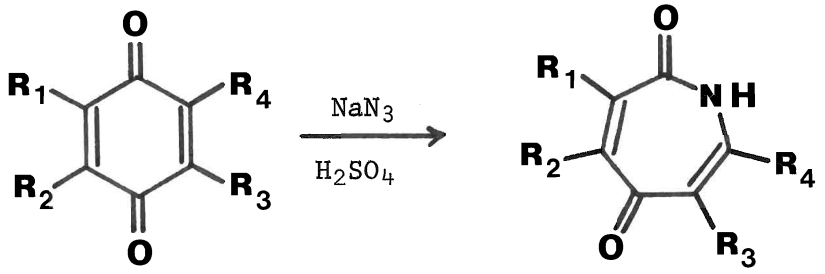


XCIV

If, however, Caronna's identification of the product of this reaction as (LXXIX) is correct, then the following scheme seems possible.

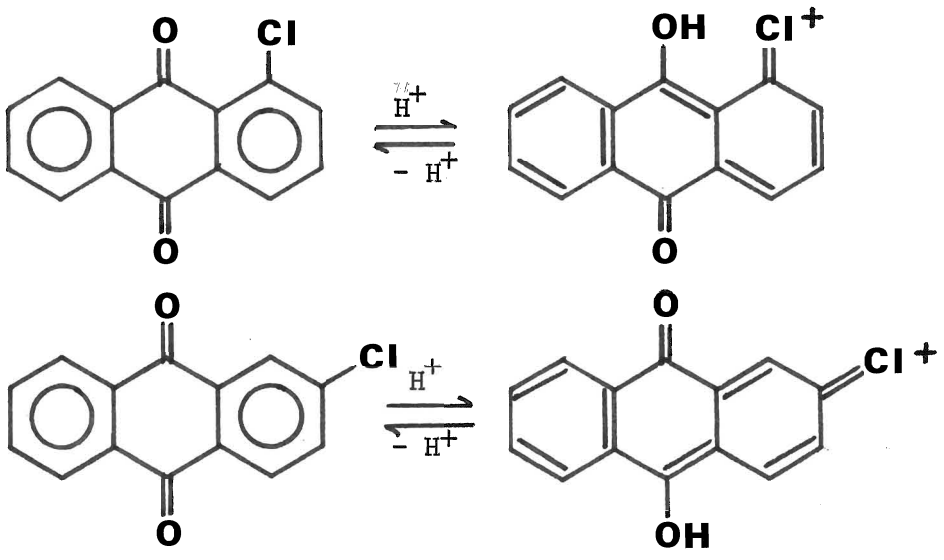


Both Folkers[35,36] and Caronna[75,76] put considerable weight on electronic effects in explaining their results and proposing mechanisms for their insertion reactions. However, in the case of assorted naphthaquinones, other workers[37,38] found Folkers' work to be in error and, in fact, obtained mixtures of the various possible azepindione isomers (e.g., a:b:c = 4:2:1).



Compound	R_1	R_2	R_3	R_4
(a)	H	Me	Benzo	
(b)	Me	H	Benzo	
(c)	Benzo		H	Me

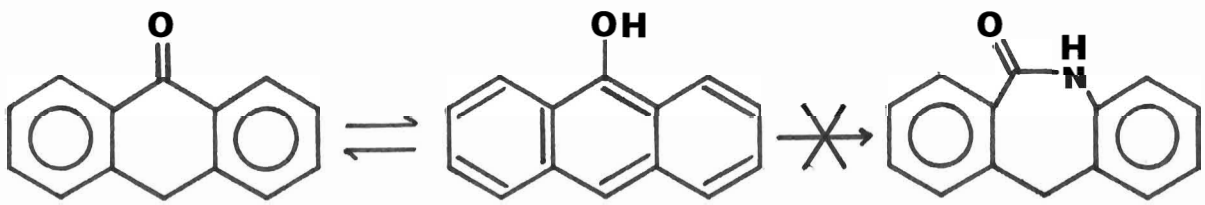
Caronna assumed initial attack at the most basic carbonyl (i.e., the one which is activated by chlorine) and migration of the most electropositive group (i.e., the one bearing the chlorine substituent). However, if the carbonyls are activated as shown below,



with the chlorine substituents stabilizing the positive charge after protonation (with subsequent attack at the 'activated' carbonyl by N_3^-) then one would not expect attack at the same carbonyl in both cases.

Although it was found in this work that initial attack may occur at the most basic carbonyl (as presumed in the case of 1-chloro-anthraquinone), subsequent migration (as indicated by the relative amounts of products obtained) was not found to be notably specific. The one case where steric hindrance at one carbonyl is much more influential in the course of the reaction was that of 1,8-dichloro-anthraquinone. There was a notable preference for attack at the carbonyl opposite the one flanked by two chlorine substituents (LXXXVI:LXXXV = 3:1). The steric influence of the chlorine substituents is also demonstrated by the resistance of (LXXXV) to base-catalyzed hydrolysis.

The unsuccessful attempt to react anthrone (XCV) under Schmidt conditions is presumably due to its transformation to the tautomeric anthrol (XCVI) which is not reactive to sodium azide[75].



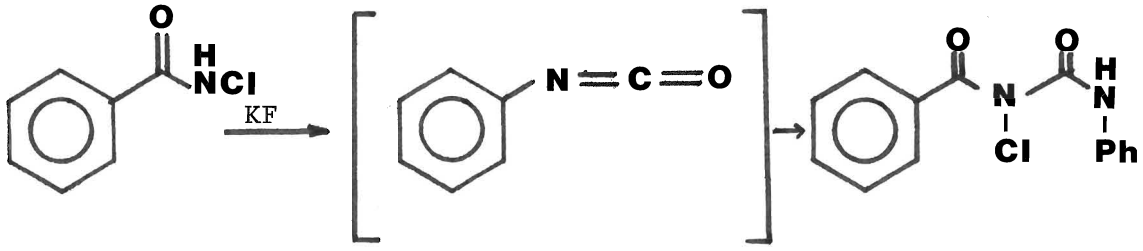
XCV XCVI

Although the identities of some of the products of the Schmidt reaction of 1- and 2- chloroanthraquinone were not assured, the method of preferential hydrolysis followed by complete cleavage and g.l.c. analysis of esters derived from the resultant acid fraction used in this work could be used to assign actual structures. This might help to resolve the question of the mechanism involved in the Schmidt reaction in these instances.

Attempted decarbonylation of an azepindione

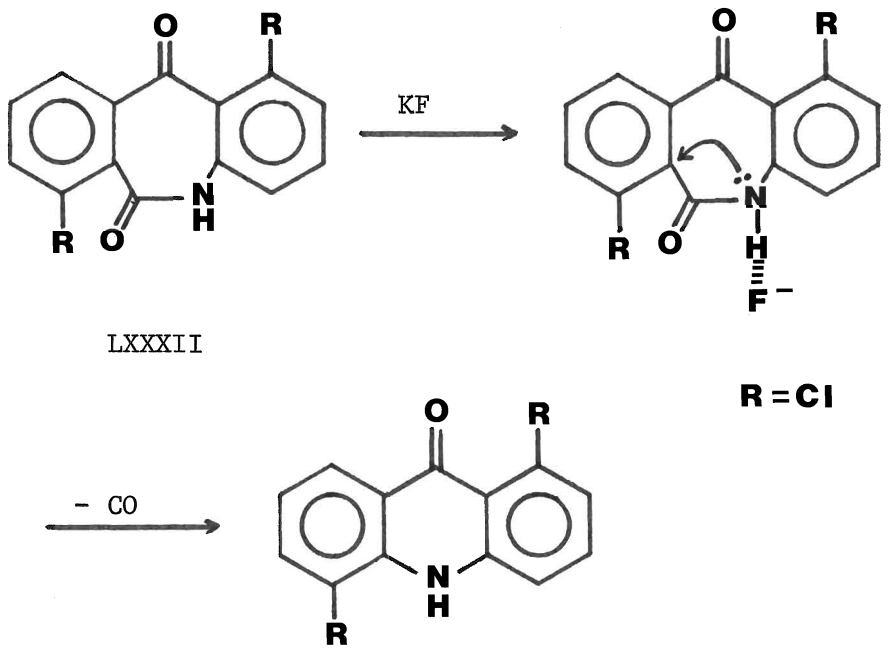
Since nitrogen functionality was easily introduced into the anthraquinone systems to give azepindiones it was tempting to investigate the possibility of expelling carbon monoxide from these types of compounds to afford substituted acridones.

The method chosen in these attempted decarbonylations was simple refluxing of the chosen azepindione in an aprotic solvent (i.e., DMSO) in the presence of potassium fluoride. This was based on the success of a previous (although not strictly analogous) reaction[77] of N-chlorobenzamide (XCVII) with potassium fluoride.



XCVII

It was hoped that fluoride ion would increase the nucleophilicity of the ring nitrogen by strongly hydrogen bonding the -NH proton. This then might allow an intramolecular rearrangement (similar to the Hofmann reaction) with resultant expulsion of CO, as shown below.



LXXXII

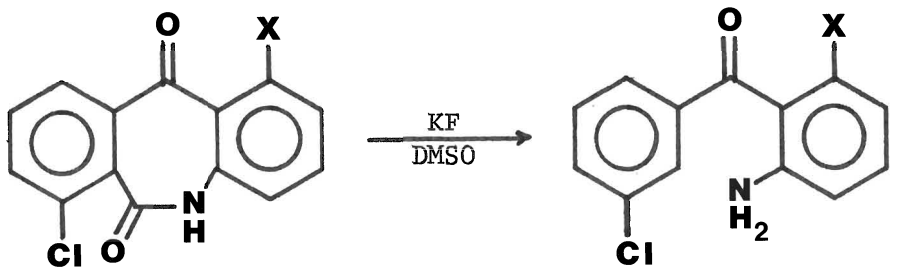
R = Cl

XCVIII

This would offer a convenient route to a number of acridone derivatives such as (XCVIII).

Time did not allow for a thorough study of these reactions and the products were not isolated in pure form. However, tentative identifications of the major products were made.

(LXXXVIII) and (LXXXII) were treated with a large excess of potassium fluoride in refluxing DMSO. The mass spectral data suggested the following results.

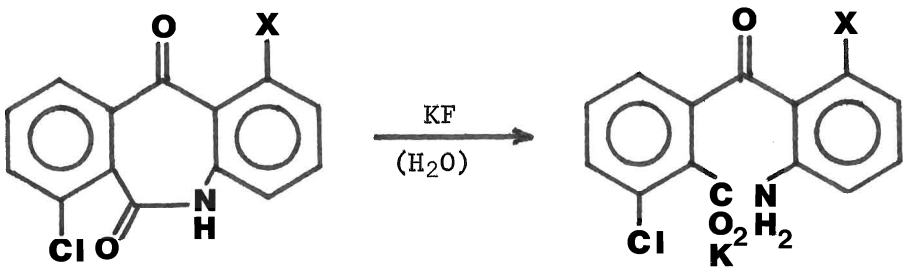


X = Cl, H

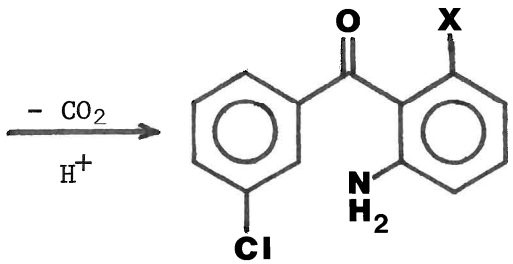
XCIX

Instead of the anticipated acridones, the reaction appeared to produce the unsymmetrical amino-benzophenone (XCIX).

The following mechanism is proposed for this reaction.



C



X = Cl, H

Potassium fluoride first acts as a base and enables the azepindiones to be hydrolyzed to the amino-acid (C) (as the potassium salt). Electron-withdrawal by the chlorine adjacent to the carboxyl-group facilitates decarboxylation, and subsequent protonation produces the benzophenone (XCIX). Potassium fluoride has been previously reported[78] to catalyze the decarboxylation of adipic acid.

Development of this type of reaction might prove useful, especially in the production of unsymmetrical amino-benzophenones which are not readily accessible by other methods. More work in this area is indicated.

Another possible method of decarbonylating suitable azepindiones might involve photochemical methods. Photo-decarbonylation of nitrogen heterocycles[79] and some benzothiophenones[80] have been reported. However, time did not allow for examination of this type of reaction.

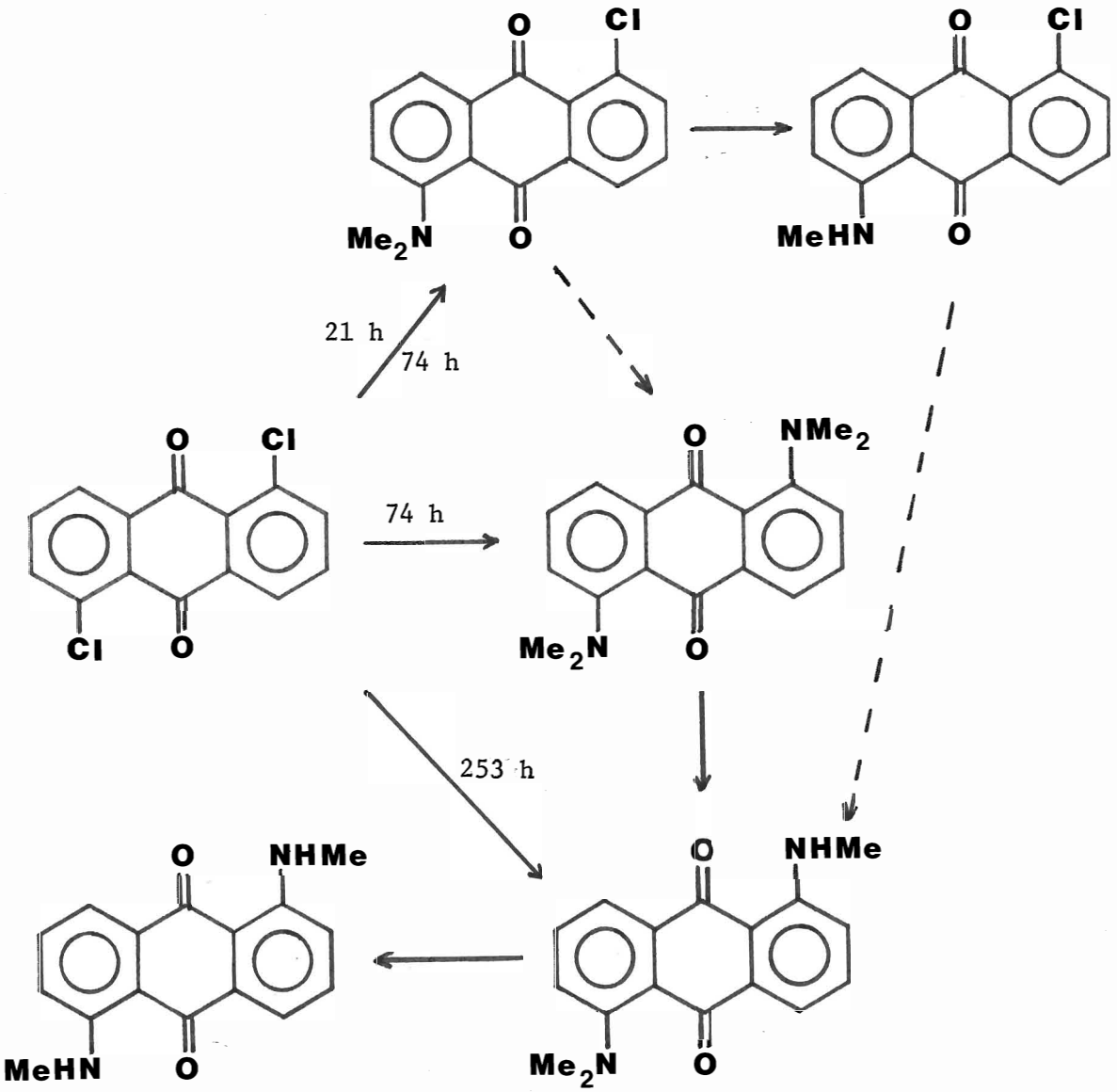
The reaction of some aryl halides and phenols with hexamethylphosphoramide (HMPA)

N-Alkylamino-anthraquinones have been prepared in the past by various methods. Hall and Hey[22] were able to obtain 1-chloro-5-methylaminoanthraquinone (after extensive purification) by heating 1,5-dichloroanthraquinone with methylamine and pyridine in a pressure bottle. The purity of their sample was questionable (no spectral data) and no yields were given. Lord and Peters[23] obtained a number of N-alkylamino-anthraquinones (including 1-chloro-5-methylaminoanthraquinone) in very low yield by refluxing 1,5-dichloroanthraquinone in dimethyl-formamide for 21 to 253 hours.(see Scheme 5).

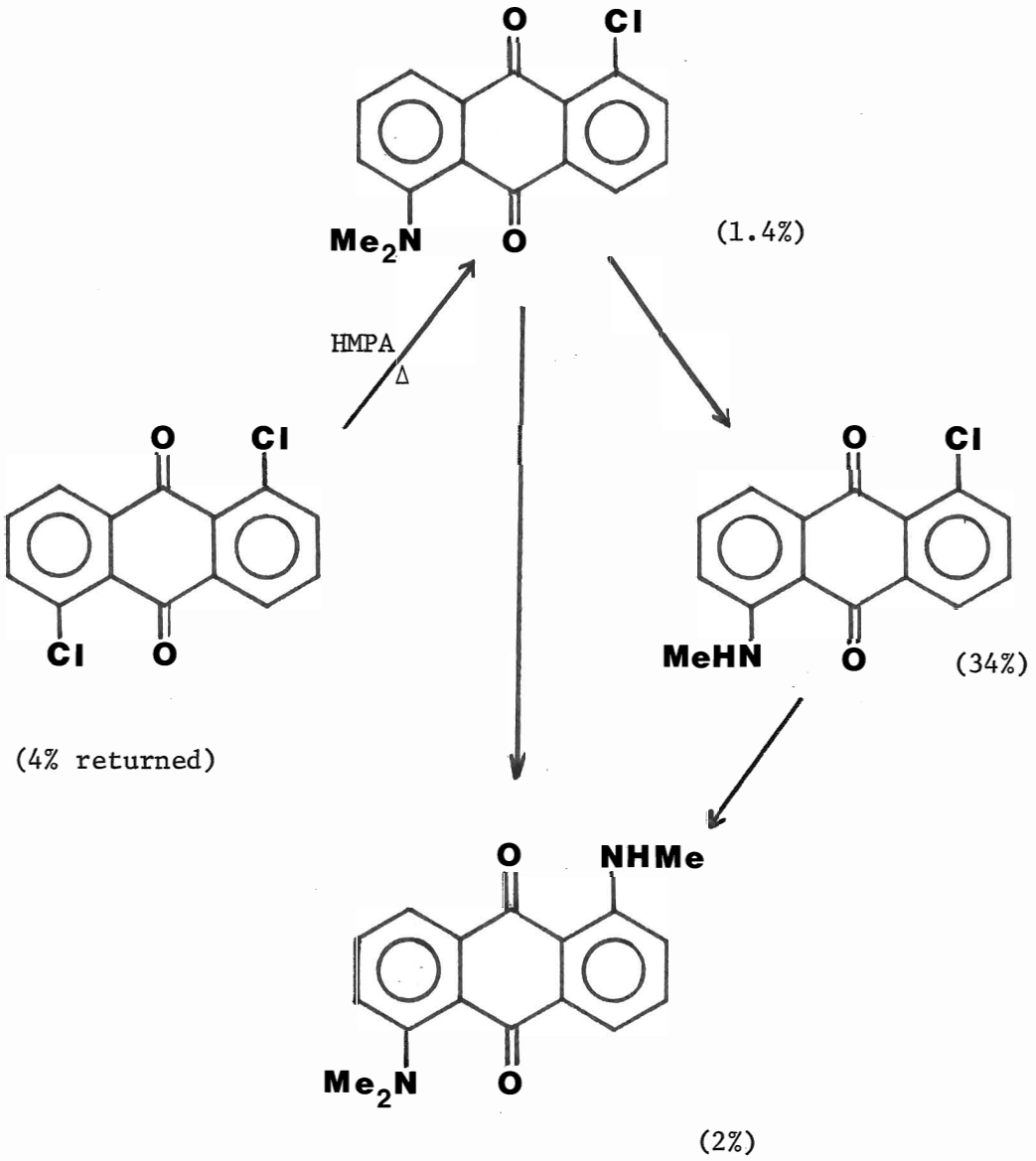
A more usable reaction for producing N-alkylaminoanthraquinones in fairly good yield (35-40%) was found to be the reaction of 1,5-dichloro-anthraquinone with refluxing N-methylformamide[21]. This reaction gave 1-chloro-5-methylaminoanthraquinone (with some starting material returned) or 1,5-bis(methylamino)-anthraquinone, depending on the reaction times used (3 and 24 hours, respectively).

Although small quantities of HMPA are known to accelerate the formation of diphenylamines from arylamines and p-chloronitrobenzene[23], HMPA has not yet been used to displace chlorine (or other halogens) nucleophilically from aryl halides.

The reaction of 1,5-dichloroanthraquinone with HMPA for 15 minutes gave a number of products as shown in Scheme 6.



SCHEME 5. Products isolated from reaction of 1,5-dichloroanthraquinone and DMF[23].



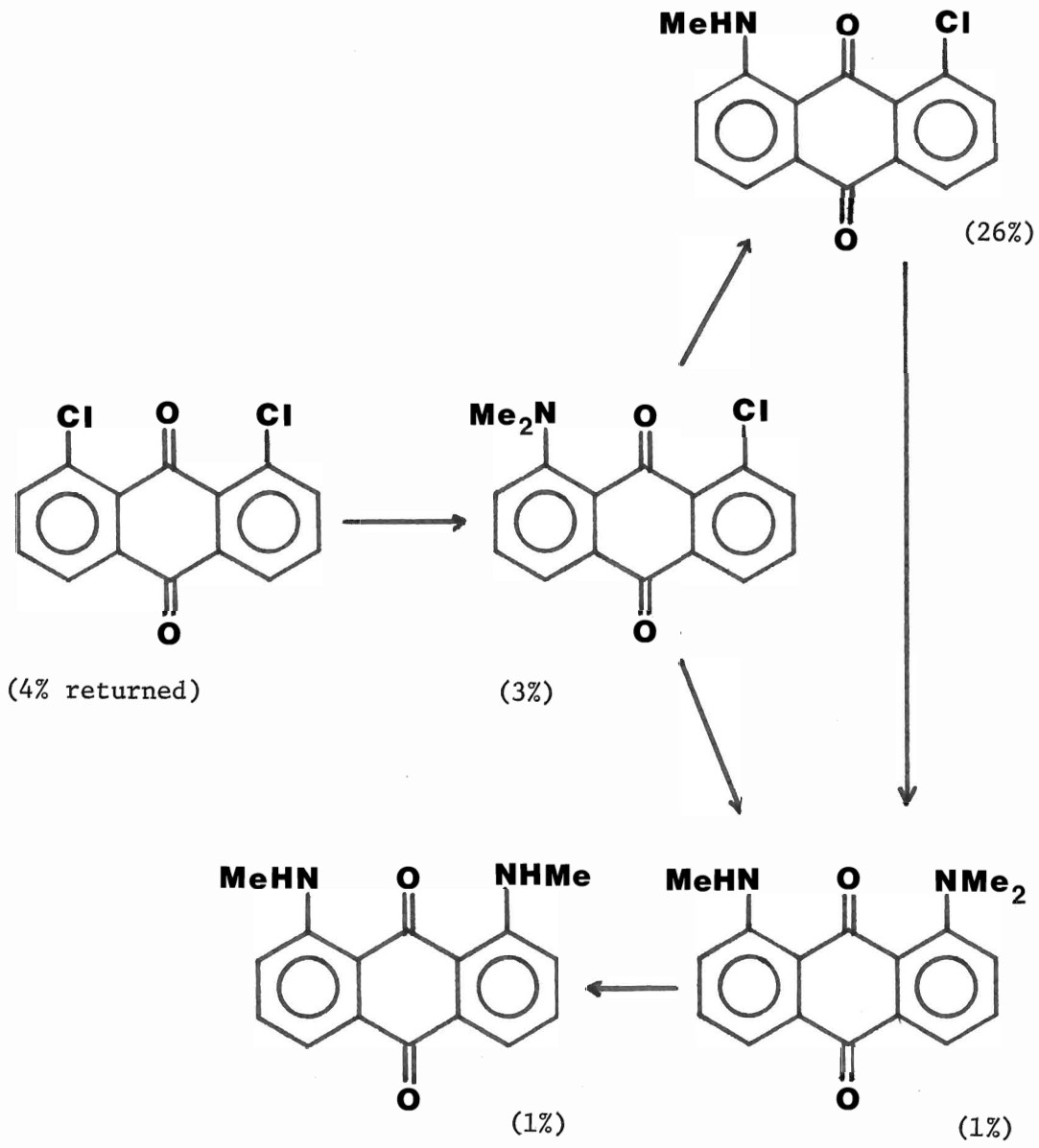
SCHEME 6. Products isolated from reaction of 1,5-dichloroanthraquinone with HMPA

These compounds were separated using a long column of silica gel with a considerable amount of dark material being retained at the top of the column. Increased reaction times caused an increase in the amount of tarry material obtained.

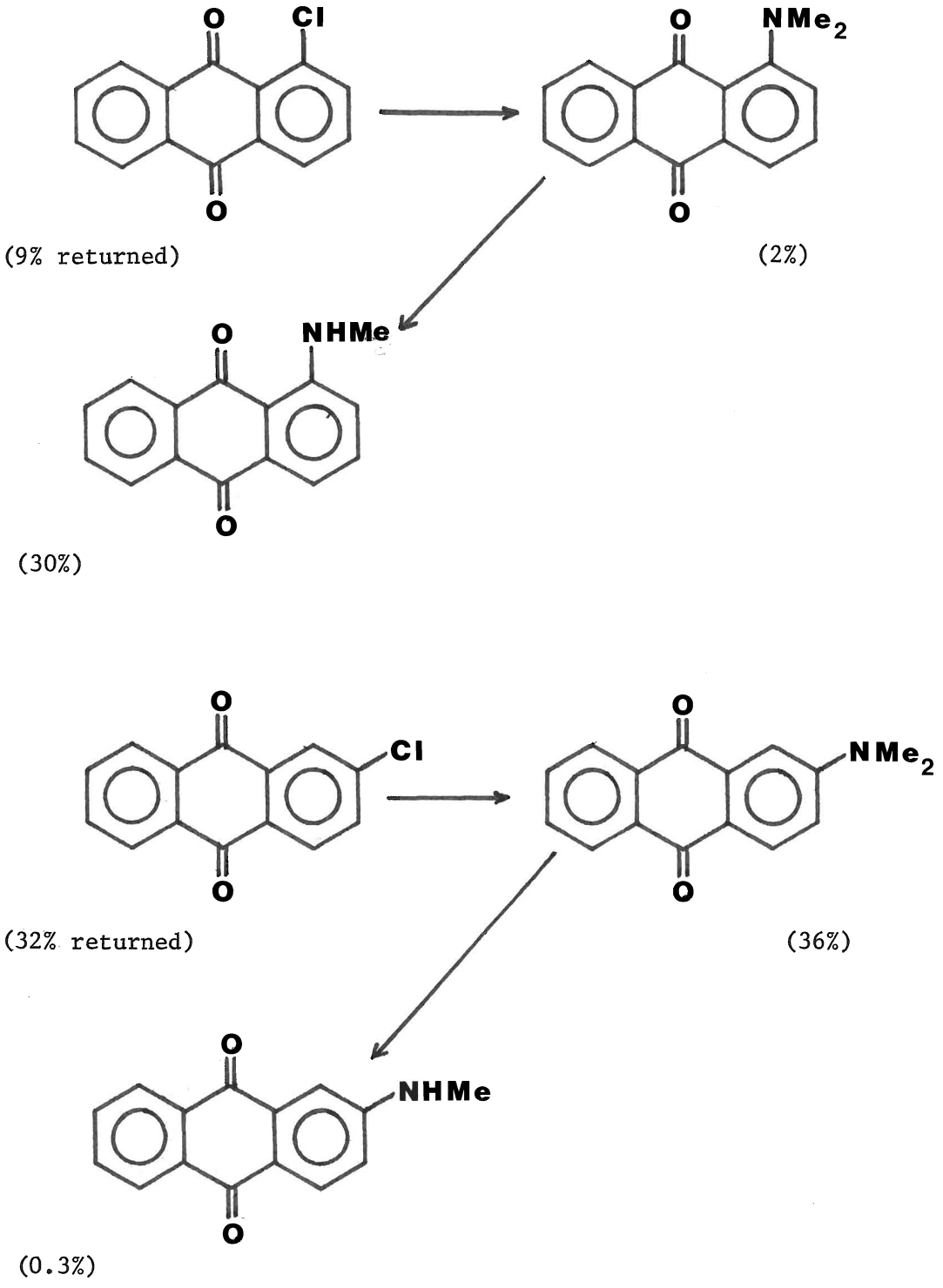
The reaction of 1,8-dichloroanthraquinone with HMPA (Scheme 7) gave analogous products to those obtained with 1,5-dichloroanthraquinone except that, in addition, a small amount (1%) of 1,8-bis(methylamino)-anthraquinone was obtained. The latter could only be isolated by rechromatographing the small mixed fraction obtained by initial chromatography.

Similarly, 1- and 2-chloroanthraquinone reacted with HMPA to give analogous products to those obtained in the other two cases (Scheme 8). As with previous minor products, 2-methylaminoanthraquinone could only be obtained in relatively pure form by rechromatography of an initial minor fraction.

The difference in reactivity of these two isomers (as indicated by reaction times and starting material returned) is most likely due to the fact that inductive activation by ortho-carbonyl groups (as in 1-chloroanthraquinone) is greater than that of para-carbonyl groups (as in 2-chloroanthraquinone)[57]. The difference in reactivity is even more pronounced in the reactions with hexaethylphosphoramide (HEPA).

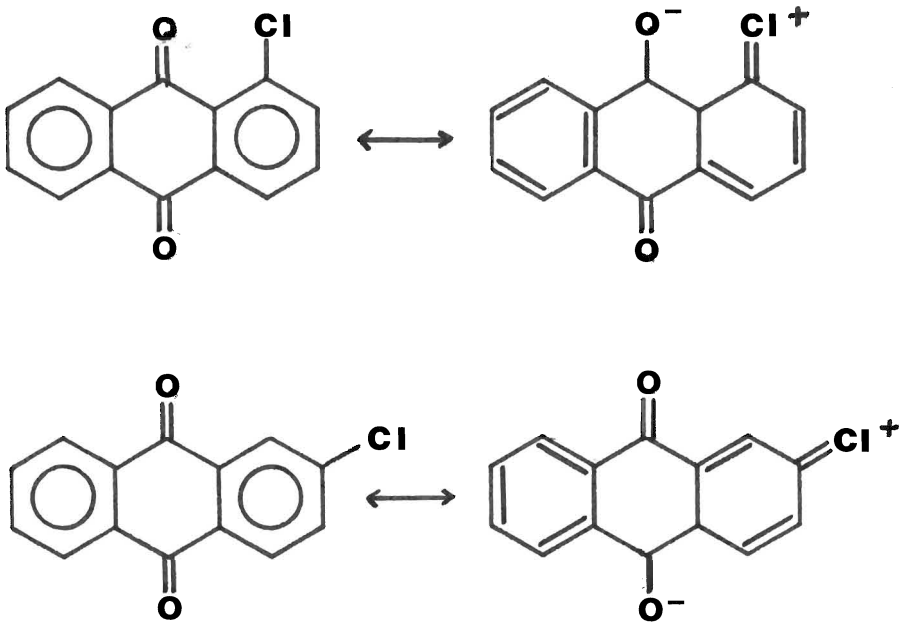


SCHEME 7. Products isolated from reaction of 1,8-dichloroanthraquinone with HMPA.



SCHEME 8. Products isolated from reaction of 1- and 2-chloro-anthraquinone with HMPA.

i.e.,

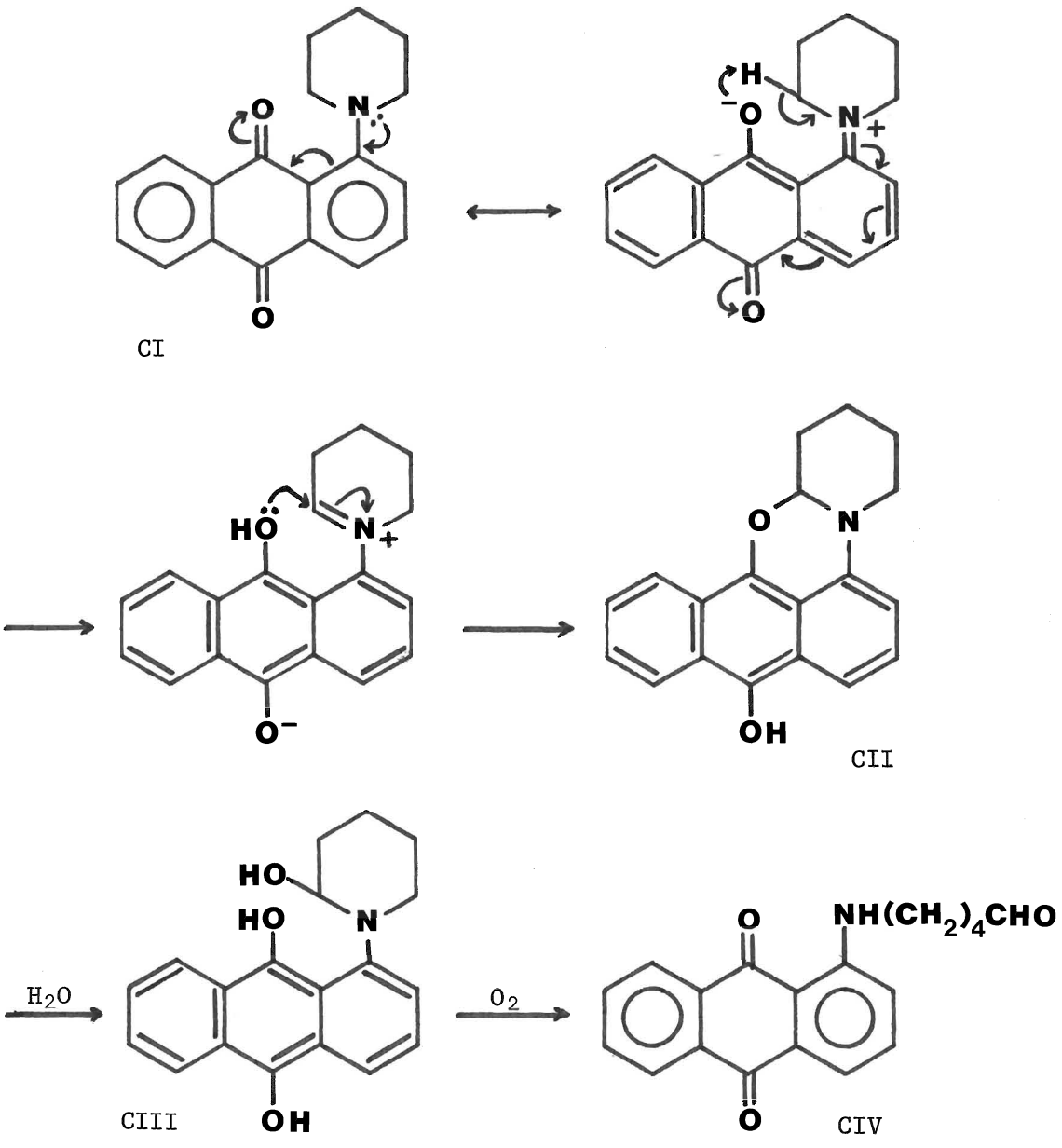


Of interest in these reactions are the demethylations which occur. T.l.c. monitoring of the reaction of 1,5-dichloroanthraquinone with HMPA shows an initial formation of 1-chloro-5-dimethylaminoanthraquinone from the starting material. However, as the reaction proceeds, 1-chloro-5-methylaminoanthraquinone is produced at the expense of 1-chloro-5-dimethylaminoanthraquinone. Eventually disubstituted species are also formed.

Fokin and his co-workers had previously observed the dealkylation of various 1-dialkylaminoanthraquinones in pyridine at 160-190°[81], although Lord and Peters[23] did not observe any dealkylation of 1-dimethylaminoanthraquinone in pyridine. Since dealkylation of 1-dimethylaminoanthraquinone occurs readily in dipolar aprotic solvents

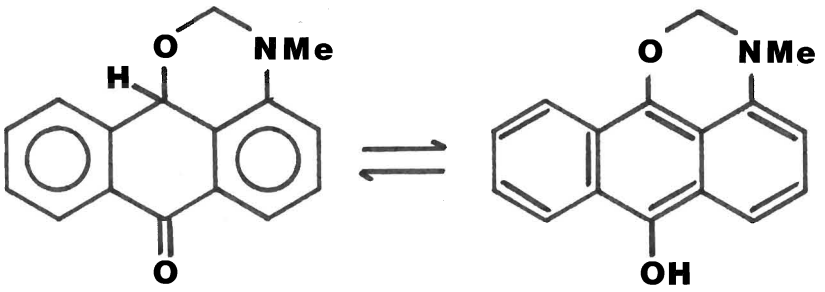
like DMF, DMSO and dimethylsulfone (DMS)[23] it is not surprising that similar dealkylations were found while using HMPA .

Fokin's group extended their work to cyclic 1-amino-anthraquinones such a 1-piperidino-anthraquinone (CI) where they observed ring opening to give an aldehyde (CIV)[82]. This was shown to be formed via (CII) and possibly (CIII), since treatment of the reaction mixture with acetic anhydride trapped (CII) as its acetate[83]. The reaction has been explained in terms of the following mechanism[84].



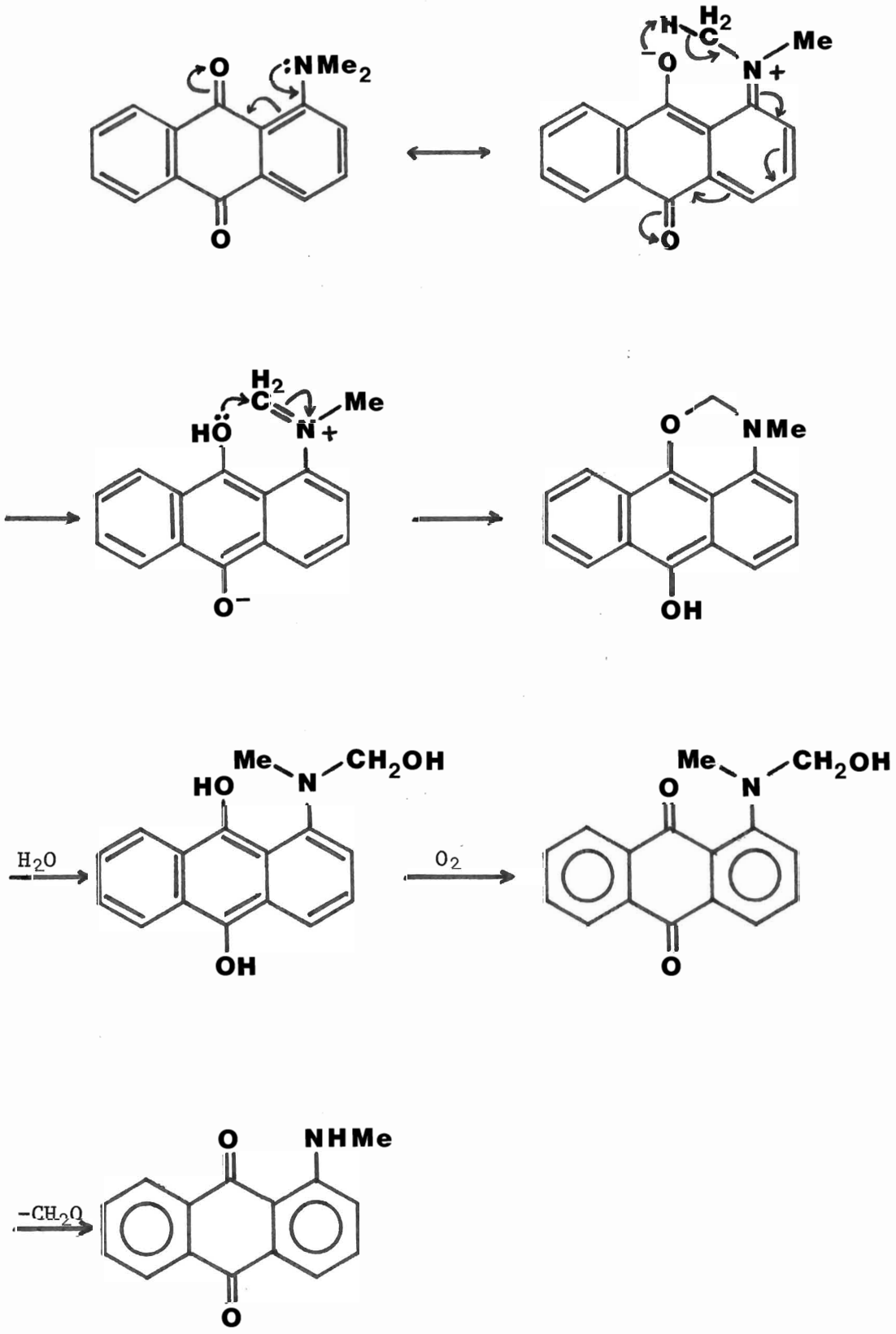
A similar type of mechanism[21] has been applied to the type of demethylations observed by Lord and Peters when reacting 1-chloro, 1,2-, 1,4-, 1,5- and 1,8-dichloroanthraquinones with dimethylformamide (DMF) (Scheme 9).

This proposal might well be experimentally substantiated, since reaction of 1-methylaminoanthraquinone with para-formaldehyde and copper powder in 70% sulfuric acid is reported to give a compound formulated as (CV)[85]. Presumably, (CV) might also be formulated as (CVI) which is the assumed reactive intermediate in the demethylation of 1-dimethylaminoanthraquinone[21].



CV CVI

Refluxing (CV) in a polar aprotic solvent would then be expected to return 1-methylaminoanthraquinone. This mechanism is consistent with the fact that no demethylation was previously observed in the reaction of 2-chloroanthraquinone with DMF[23].

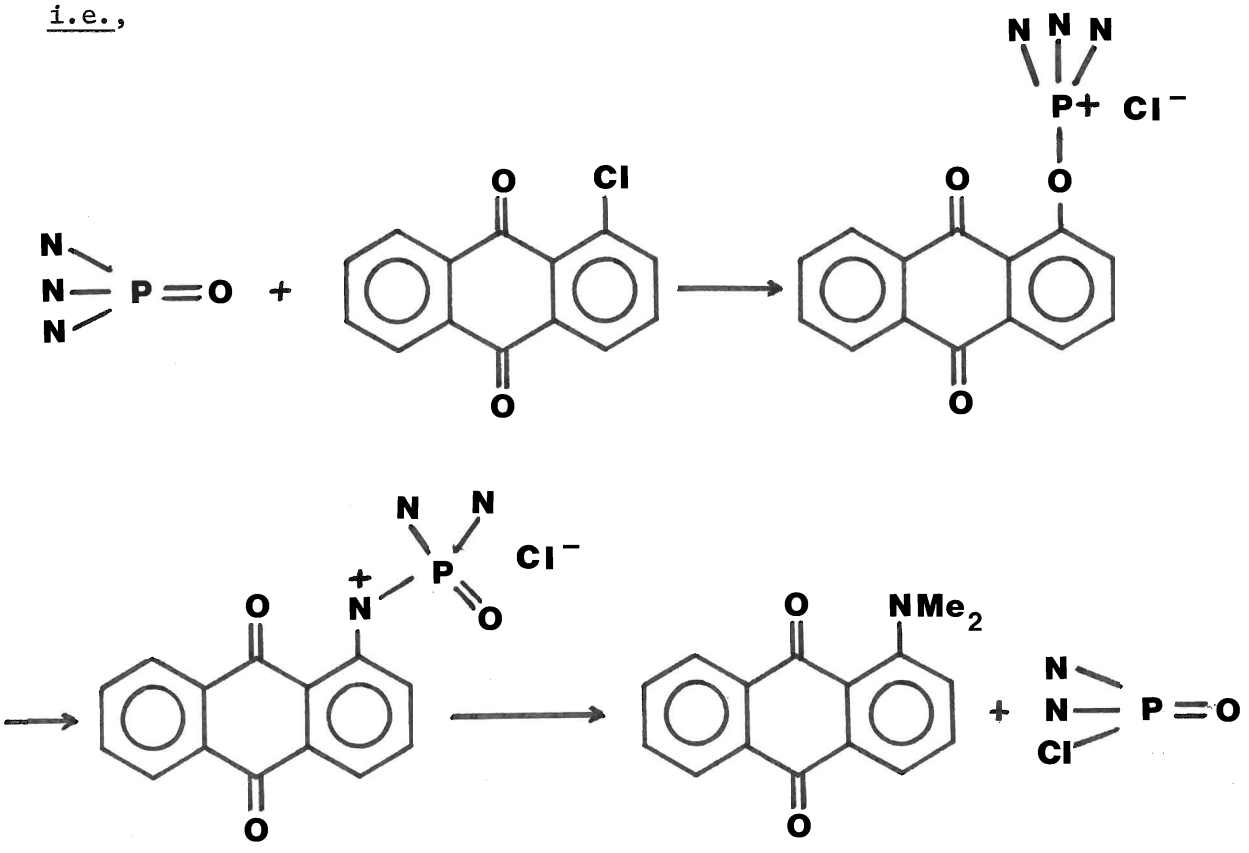

O
:NMe2
O
H2
C
Me
N+
O
O
H2
C
Me
HO
N+
O−
O
NMe
OH
Me
N
CH2OH
HO
H2O
OH
Me
N
CH2OH
O
O2
O
-CH2O
NHMe
O

SCHEME 9[21].

However, when 2-chloroanthraquinone was reacted with HMPA, a small amount (<1%) of 2-methylaminoanthraquinone was found, although the main product (36%) was 2-dimethylaminoanthraquinone. Although the sample of the demethylated product was slightly impure (m.p. and mass spectrum), its identity was confirmed by ^{1}H-n.m.r. which showed the presence of a methyl-group coupled to a D_2O-exchangeable proton. What appears to be a similar dealkylation occurs when reacting 2-chloroanthraquinone with HEPA to give 2-ethylaminoanthraquinone (identified by mass spectrum) as well as 2-diethylaminoanthraquinone. Dealkylation in this case cannot be rationalized in terms of the mechanism assuming a cyclic intermediate, as in previous examples.

The reaction of HMPA (and HEPA) with chloroanthraquinones is presumed to take place by a mechanism which is analogous to the reaction of acyl chlorides,

<u>i.e.</u>,

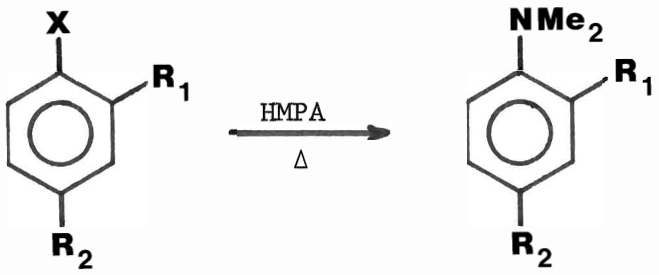


Since the production of dimethylamine was observed during the course of the reaction, the possibility was considered that it was acting as the aminating agent. This has been suggested as the mechanism for the production of dimethylaminopentafluorobenzene from hexafluorobenzene in DMF[86], since dimethylamine is known to accumulate in DMF[87].

Dimethylamine did not seem to be produced simply by thermal decomposition of HMPA. It may slowly accumulate in HMPA (as with DMF) and/or be produced by hydrolysis of chlorophosphoramides or other HMPA derivatives formed furing the course of the reaction. Past reactions using dimethylamine to substitute anthraquinones required extended reaction times[22,88]. Since the reactions in this work proceeded very quickly, the proposed mechanism is thought to be more likely than a mechanism involving dimethylamine.

Since it was found that chloroanthraquinones reacted quite readily with HMPA, it was considered likely that other suitably activated aryl halides would also react, in spite of the fact that HMPA was previously considered "inert" to such reactions[50]. The reactants chosen and products obtained are summarized in Scheme 10.

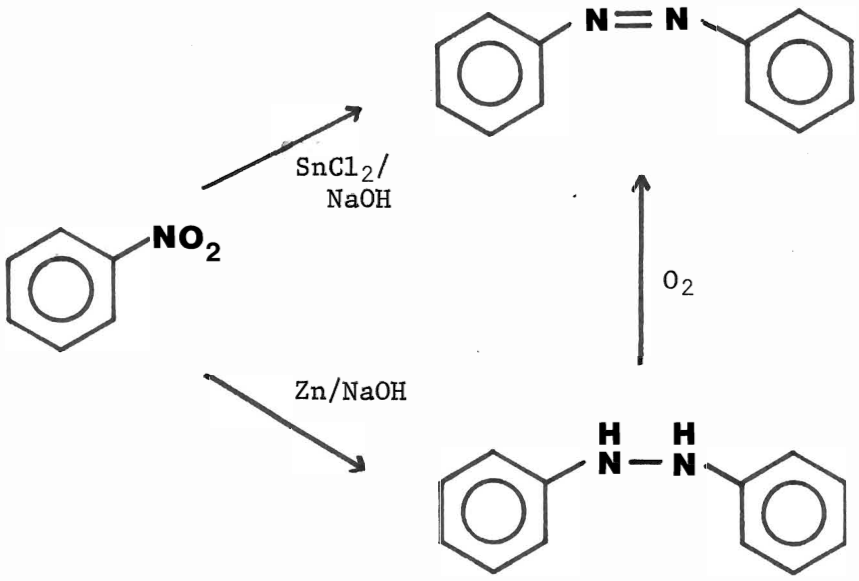
Two exceptions to -Cl displacement by $-NMe_2$ were found. 3-Chloronitrobenzene gave an anomalous reaction to give a small amount of 3,3'-dichloroazobenzene (2%) and an even smaller amount of 4-dimethylaminonitrobenzene (<1%) together with tarry material which adsorbed strongly to silica gel. It is not clear whether 4-dimethylaminonitrobenzene was produced by some type of rearrangement or by reaction of HMPA with an undetectable trace of 4-chloronitrobenzene in the starting material. At this point the latter seems more probable.



	X	R_1	R_2
(i)	Cl	H	NO_2
(ii)	Br	H	NO_2
(iii)	F	H	NO_2
(iv)	Cl	NO_2	H
(v)	Cl	NO_2	NO_2
(vi)	F	NO_2	NO_2

SCHEME 10. Products from reaction of aryl halides with HMPA.

A reductive coupling reaction of the type required to give 3,3'-dichloroazobenzene from 3-chloronitrobenzene has not been previously observed in HMPA. However, deoxygenation of nitro-compounds by tervalent phosphorus reagents has been reported[89] to give nitrene intermediates which can couple to give azo-compounds. In the past, azo-compounds have been prepared by the action of $SnCl_2$/NaOH on aromatic nitro-compounds. Hydrazo-compounds have been obtained by Zn/NaOH reduction and these are often easily oxidized in air to the corresponding azo-compounds[90].

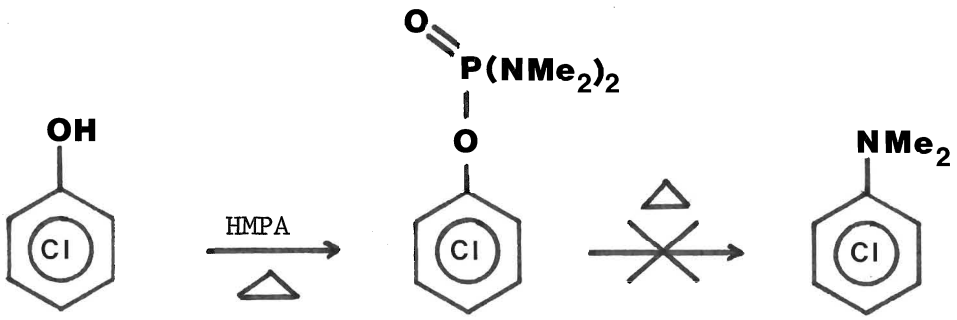


Reductions of this type are usually produced by the action of a metal or a metal salt in basic solution[90]. Although the HMPA reaction mixture is basic, no metals were present and the mechanism for the observed reduction is not clear.

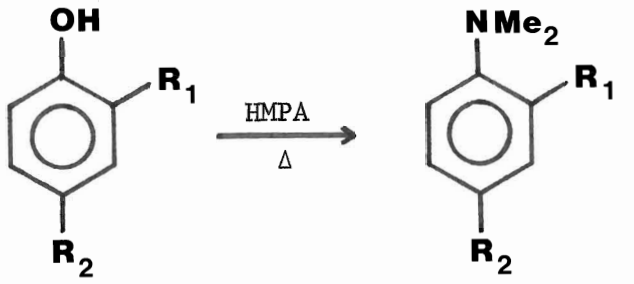
It was found that 4-chloroaniline did not undergo any reaction with HMPA and this, together with the previous case, seems to indicate that the reaction requires an activating group such as $-NO_2$ in the ortho or para positions.

The fact that HMPA has been used to amidate carboxylic acids[47] and that it can form stable complexes with phenols indicated that suitably substituted phenols might undergo nucleophilic displacement of -OH by $-NMe_2$. This was found to be the case with a number of phenols, as summarized in Scheme 11.

A unique reaction was found in the case of pentachlorophenol. On heating in HMPA the phosphorodiamidate (CVII) was produced in good yield (67%). Subsequent refluxing of the compound in HMPA did not give any dimethylaminopentachlorobenzene (CVIII).



CVII CVIII



	R_1	R_2
(i)	H	NO_2
(ii)	NO_2	H
(iii)	NO_2	NO_2

SCHEME 11. Products from reaction of phenols with HMPA.

While studying the reaction of benzyl alcohols with HMPA to give benzyldimethylamines, Monson[49] suggested the following reaction pathway by analogy with the previously explained reaction of N,N-dimethylsulfamates[91];

$$ArCH_2OH + (Me_2N)_3P{=}O \longrightarrow ArCH_2O\text{-}\underset{\underset{O}{\|}}{P}(NMe_2)_2 + Me_2NH\uparrow$$

$$\longrightarrow ArCH_2^{+}\ {}^{-}O\text{-}\underset{\underset{O}{\|}}{P}(NMe_2)_2 \longrightarrow ArCH_2\text{-}\overset{+}{N}Me_2 \quad \begin{matrix} | \\ O{=}P\text{-}NMe_2 \\ | \\ O^{-} \end{matrix}$$

$$\longrightarrow ArCH_2NMe_2 + \text{pyrophosphate}(Me_2NH_2)_2H_2P_2O_7$$

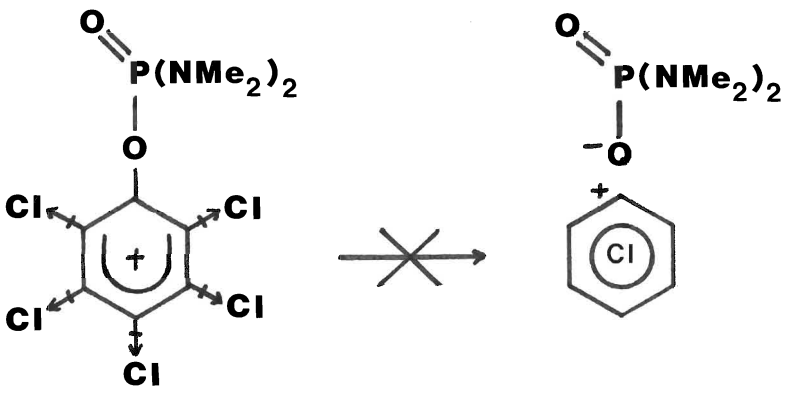
The formation of a pyrophosphate linkage of the type found above has also been reported in the thermal decomposition of alkyl tetraethyl-phosphorodiamidates ($R\text{-}OPO(NEt_2)_2$)[92].

Although the phosphorodiamidate (CVII) did not rearrange under initial reaction conditions, its production experimentally substantiates the previously proposed reaction mechanism. Two reasons may be forwarded to explain why (CVII) remains as a stable product rather than a reactive intermediate in the pathway from a phenol to a dimethylaniline;

(i) the adjacent chlorines may sterically hinder the rearrangement of the bulky phosphorodiamidate to the dimethylaniline;

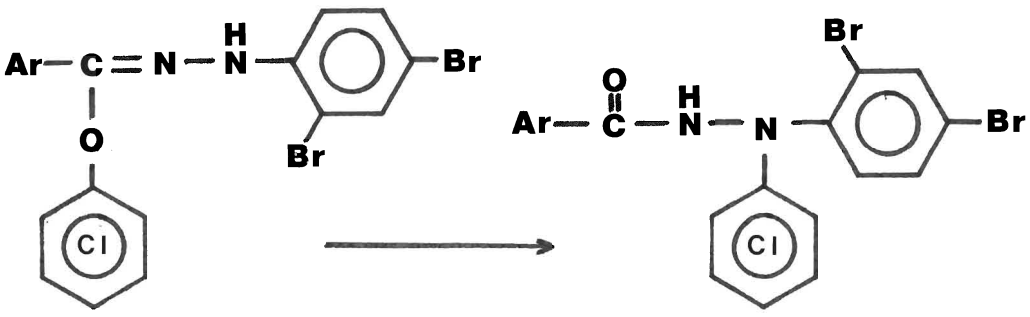
(ii) the electron-withdrawal caused by five chlorines makes the bond polarization required for rearrangement unfavourable;

i.e.,



Steric hindrance in perchlorobenzene derivatives has been reported[93] and is apparently due to the fact that the chlorines occur 25° out-of-plane with the ring (alternating above and below the plane of the ring)[94].

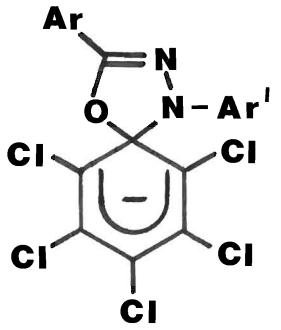
In contrast, rearrangements of pentachlorophenol derivatives such as (CIX), are known to occur readily under basic conditions[95].



CIX CX

However, this Smiles rearrangement is thought to be intramolecular and proceed through a five-membered cyclic transition state (CXI).

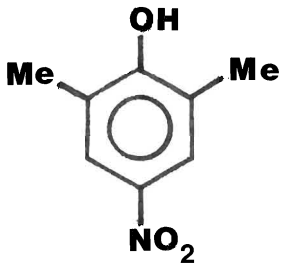
The inductive stabilization of a negative charge by the electron-deficient ring facilitates rearrangements to (CX)[95].



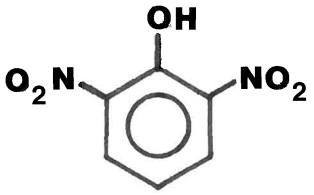
CXI

Stabilization of a positive charge would, however, be required for (CVII) to rearrange following bond polarization and this could not occur in such an electron-deficient ring system.

It may be argued that the 2,4-dinitrophenyl systems, which react readily to give 2,4-dinitrodimethylaminobenzene, are also governed by approximately comparable electron-withdrawal from the ring. This suggests that a combination of steric and electronic effects may be in operation in the pentachlorophenyl system, thereby increasing the energy barrier to rearrangement. Further work (perhaps with phenols like CXII and CXIII) is required to clarify the effects steric hindrance may have on the reaction of HMPA with substituted phenols.



CXII



CXIII

The reaction of HMPA with aryl halides offers a useful route to N-dimethyl-arylamines and N-methylaminoanthraquinones; the former also being available in one step by the reaction of phenols with HMPA.

EXPERIMENTAL

General

Melting Points

All melting points were measured on a Kofler hot stage microscope. Quoted values are uncorrected.

Thin Layer Chromatography

This was done using Silica gel IB2-F slides from J. T. Baker Chemical Co. Preparative t.l.c. was carried out using similar 20 x 5 cm sheets. The t.l.c. slides were developed with chloroform and subsequently examined under u.v. light.

Column Chromatography

Except where indicated otherwise, all columns were packed with Silica gel (60-200 mesh) and eluted with benzene. Microcolumns were prepared using Fisher disposable pipettes. Dry column chromatography[96] was used in all cases.

Infra-red Spectra

Spectra of all compounds were obtained using potassium bromide discs on a Perkin-Elmer 237B grating infra-red spectrophotometer. Abbreviations used are: s = strong, w = weak, sh = sharp, br = broad.

N.M.R. Spectra

The spectra were obtained on a Bruker WP60 nuclear magnetic resonance spectrometer. All chemical shifts are listed as δ values using tetramethylsilane as internal standard (δ 0.0). The ^{31}P spectra were run at 24.29 MHz using H_3PO_4 as external standard. The solvents used are listed in the text. The following abbreviations are used: s = singlet, t = triplet, m = multiplet, d = doublet, q = quartet, br = broad.

Mass Spectra

An AEI-MS30 double beam, double focusing mass spectrometer was used to obtain the reported spectra. The results are quoted as m/e values for the lowest isotopic species except where isotopic ratios helped to indicate the identity of the fragment.

Yield

Yields are based on material used for the reaction.

Microanalyses

These were done by Dr. F. Pascher, Mikroanalytisches Laboratorium, Buschstr. 54, 5300 Bonn, Germany.

Solvents

Hexamethylphosphoramide (HMPA) was stored over 13X molecular sieves. Tetrahydrofuran was dried and purified by the benzophenone ketal[97] method. t-Butylbenzene was purified by fractional distillation

at reduced pressure and was stored over sodium wire. Other solvents were purified when necessary by standard methods[97,98]. Ligroine refers to the fraction boiling in the range 30-60°.

Preparation of potassium amide in liquid ammonia

Commercial liquid ammonia was introduced into a 3-necked flask. Several small chips of sodium were added until a permanent blue coloration resulted. The ammonia was then distilled (with a water bath) into a second 3-necked flask fitted with a dry-ice condenser, a mechanical stirrer and a dropping funnel.

The ammonia was condensed using dry ice-acetone after which a small chip of potassium was added. A small crystal of ferric nitrate was then added followed by the requisite amount of potassium. Stirring was maintained throughout until the blue coloration gave way to the grey of potassium amide.

Preparation of potassium t-butoxide

Potassium t-butoxide was prepared immediately before it was used. Anhydrous t-butanol was prepared by refluxing t-butanol over sodium wire for about 2 hours followed by distillation.

The anhydrous solvent was introduced into a flask with a reflux condenser fitted with a drying tube. The requisite amount of potassium was slowly added and the mixture was stirred during reflux until all the potassium had reacted. The excess t-butanol was then removed at reduced pressure (≃20 mm) to give potassium t-butoxide as a white solid which could be sublimed.

When water was added in small amounts to prepare a potassium t-butoxide-water reagent, it was added as a 10% (v/v) solution in 1,2-dimethoxyethane.

Attempted preparation of 1-chloro-5-nitroanthraquinone (XLIV)

1-Chloroanthraquinone (1.0 g, 0.004 mole) was dissolved in concentrated H_2SO_4 (25 ml) and concentrated HNO_3 (5 ml) was added dropwise to the stirred solution while the temperature was kept at 70-80°. The reaction mixture was maintained in this manner for 15 minutes and was then slowly added to 250 ml of cold water. The resulting precipitate was collected by filtration, washed with water and then a small amount of cold acetone and dried. The resulting yellow solid (1.1 g) was crystallized twice from chlorobenzene (charcoal) to give 1-chloro-4,X-dinitroanthraquinone (XLIV) (0.8 g, 60%) as bright yellow crystals, m.p. >320°. (Calcd. for $C_{14}H_5N_2O_6Cl$: C, 50.55; H, 1.52; N, 8.42. Found: C, 50.50; H, 1.63, N, 8.37%.); mass spectrum m/e 334 (M^+ ^{37}Cl) (28), 332 (M^+) (100%), 302 (M-NO) (10), 297 (M-Cl) (7), 273 (M-NO-HCO) (12), 256 ($M-NO_2$) (24), 228 ($M-NO_2-CO$) (11), 200 ($M-NO_2-2CO$) (16), 184 (18), 172 (29), 149 (184-Cl) (30), 137 (172-Cl) (31); ν_{max} 3060 (w), 1687 (s, br), 1545 (s, br), 1400, 1375 (s), 1310 (s, br), 1250 (s, br), 1150, 1135, 875 (sh), 840 (s, sh), 820 (sh), 800 (sh), 720 (sh), 695 (sh), 675 (sh) cm^{-1}; ^1H-nmr ($CDCl_3$) 8.6-8.2 (m).

Preparation of 1-amino-5-chloroanthraquinone (XLV)

1,5-Dichloroanthraquinone (10.0 g, 0.036 mole) was heated in DMSO (100 ml) until it just dissolved. Then NaN_3 (7.0 g, 0.11 mole) in water (25 ml) was added dropwise over 5 minutes and the solution refluxed for an additional 30 minutes. After cooling, the solution was poured into water (600 ml) and the resulting solution acidified (concentrated H_2SO_4). This gave a suspension which was allowed to stand overnight and then filtered to give a chocolate-brown solid (9.4 g). After air-drying, the solid was pulverised and extracted with chloroform using a Soxhlet extractor. This gave an orange-brown solution and a black insoluble carbonaceous residue (3.1 g). The chloroform solution was concentrated and chromatographed (benzene:ligroin = 1:1) to give two main fractions.

Fraction 1 was found to be 1,5-dichloroanthraquinone (0.43 g, 4%). It was identical with the starting material (R_f, mass spectrum).

Fraction 2, after evaporation and crystallization (acetic acid/water) gave 1-amino-5-chloroanthraquinone (XLV) (3.01 g, 33%) as brick-red needles, m.p. 204-208° (lit.[99] 210°); mass spectrum m/e 259 (M^+ ^{37}Cl) (38), 257 (M^+) (100%), 229 (M-CO) (25), 223 (M + 1-Cl) (38), 201 (M-2CO) (13), 195 (M + 1 -CO-Cl) (8), 173 (M-2CO-H-HCN) (5), 166 (M-2CO-Cl) (17), 139 (M-2CO-Cl-HCN) (25); ν_{max} 3440 (br), 3310 (w), 2910 (w), 1670, 1635, 1605, 1575 (w), 1540, 1460 (w), 1260, 800, 760 (sh), 730 (w), 700 (sh) cm^{-1}. A large amount of dark material was retained by the column and was not further investigated.

Alternate preparation of 1-amino-5-chloroanthraquinone (XLV)

1,5-Dichloroanthraquinone (2.0 g, 0.0072 mole) was dissolved in DMSO (50 ml) with stirring at 90-100° and anhydrous KF (5.0 g 0.086 mole) was added. Ammonia was then slowly bubbled through the stirred solution (by means of a glass sinter) for 2 hours . The mixture was then allowed to cool and poured into water (400 ml). After acidification with concentrated H_2SO_4, a precipitate appeared and was collected by filtration, washed with water and air-dried to yield a reddish-brown solid (1.9 g). Chromatography gave two major fractions.

Fraction 1 gave 1,5-dichloroanthraquinone (0.15 g, 8%) as a yellowish solid; it was identical with the starting material.

Fraction 2 gave, after evaporation and crystallization (acetic acid/water) 1-amino-5-chloroanthraquinone (0.65 g, 35%); it was identical (m.p., R_f and mass spectrum) with the previously obtained sample. Several other components of lower R_f were not investigated.

Reaction of 1-amino-5-chloroanthraquinone with potassium amide in liquid ammonia

1-Amino-5-chloroanthraquinone (1.0 g, 0.004 mole) in dry tetrahydrofuran (75 ml) was added dropwise over 20 minutes to a stirred solution of potassium amide, prepared from potassium (3.1 g, 0.08 atom) and redistilled liquid ammonia (400 ml). This mixture was stirred with a mechanical stirrer for 5 hours. Ammonium chloride (5.0 g) was then carefully added together with ether (50 ml). The ammonia was then allowed to evaporate overnight.

The residue was treated with 2N hydrochloric acid (4 x 50 ml) and extracted with ether (3 x 100 ml) to give an acidic and an ethereal solution. The acidic solution was basified with 40% (w/v) NaOH, but no chloroform soluble material was precipitated. This solution was discarded.

The ethereal solution was extracted with 40% (w/v) NaOH (3 x 50 ml) (this yielded no solid on acidification), washed with water, dried (Na_2SO_4) and the solvent removed to give a dark red solid (0.7 g). This afforded 1-amino-5-chloroanthraquinone (0.6 g, 60%) as red needles (acetic acid/water) which were identical (m.p., R_f and mass spectrum) with the starting material. None of the desired acridone-1-carboxylic acid (m/e 239) was observed.

Reaction of 1-amino-5-chloroanthraquinone with potassium t-butoxide in t-butylbenzene

A mixture of 1-amino-5-chloroanthraquinone (1.05 g, 0.004 mole), potassium t-butoxide (1.34 g, 0.012 mole) (from 0.5 g potassium in t-butanol) and t-butylbenzene (35 ml) was refluxed under nitrogen for 12 hours.

The hot solution was then poured into an evaporating dish and the solvent allowed to evaporate overnight.

The resulting residue was taken up in water (200 ml) and extracted with chloroform (4 x 50 ml). The chloroform extracts were combined, washed (H_2O) and dried (Na_2SO_4). Removal of the solvent gave a reddish brown solid (0.5 g). After crystallization (acetic acid/water) this was identified as 1-amino-5-chloroanthraquinone (0.4 g, 38%) and was found to be identical with the starting material (R_f, mass spectrum).

The aqueous solution was acidified (concentrated H_2SO_4) and extracted with chloroform (4 x 50 ml). The chloroform solution was washed with saturated aqueous potassium bicarbonate (4 x 100 ml) and then washed with water and dried. Evaporation gave an additional amount of impure (t.l.c.) 1-amino-5-chloroanthraquinone (0.3 g, 29%; 67% total) which was identical with the starting material.

The bicarbonate washings were carefully acidified with concentrated HCl and then extracted with chloroform (2 x 50 ml). After standard washing and drying of the organic solution the solvent was evaporated and the resulting solid crystallized from ethanol/water. This afforded

1-amino-5-hydroxy-anthraquinone (XLVI) (0.025 g, 3%) as dark red needles, m.p. 255-260° (lit.[100] 215-216°). (Calcd. for $C_{14}H_9NO_3$: C, 70.29; H, 3.79; N, 5.86; Found: C, 62.11; H, 5.60; N, 4.31.); mass spectrum m/e 240 (M^+ ^{13}C) (18); 239 (M^+) (100%), 238 (M-H) (25), 210 (M-HCO) (11), 182 (M-HCO-CO) (9), 154 (M-HCO-2CO) (12), 127 (154-HCN) (7); metastable observed at m/e 186, assigned to $[M]^+ \longrightarrow [M\text{-}HCO]^+ + HCO^{\cdot}$ (m^*_{obs}: m/e 186; m^*_{calc}: m/e 186.3); ν_{max} 1640, 1590, 1540, 1330, 1280, 1255, 820 (br), 712 (s, sh) cm^{-1}.

The mass spectrum and R_f were identical with those of an authentic sample of 1-amino-5-hydroxyanthraquinone, prepared by a non-ambiguous method.

Attempted preparation of an acridine-carboxylate from a substituted anthraquinone

(i) 1-p-Toluidino-5-chloro-anthraquinone (LXI)

1,5-Dichloroanthraquinone (5.0 g, 0.018 mole) was heated to reflux in a melt of p-toluidine (20 g) for 15 minutes. The mixture was allowed to solidify and was then taken up in ethanol (50 ml). Filtration of this suspension gave a red-black residue (4.7 g) and an ethanolic solution from which unused p-toluidine could be crystallized. Chromatography of the solid material gave two major fractions.

Fraction 1 gave, after evaporation and crystallization (pyridine), 1,5-bis(p-toluidino)-anthraquinone (LXII) (0.25 g, 3.3%) as black needles with a golden lustre, m.p. 301-305° (lit.[101] m.p. not available); mass spectrum m/e 420 (M^+ $2^{13}C$) (9), 419 (M^+ ^{13}C) (39), 418 (M^+) (100%), 417 (M-H) (8); ν_{max} 1625, 1595, 1570, 1515 (br), 1355, 1320 (w), 1305 (5), 1265, 1255, 1170 (sh), 810, 795 (sh), 765 (sh), 705 (sh), 695 (w) cm^{-1}; ^{1}H-nmr (d_6-DMSO) 8.1 (br s, 2H), 7.7-7.3 (m, 6H), 7.2 (s, 8H), 2.4 (s, 6H).

Fraction 2 gave a red-purple solid which was rechromatographed (toluene) to give 1,5-bis(p-toluidino)-anthraquinone (0.1 g, 1.3%; total yield 5%) as the first fraction; it was identical with the previously obtained sample. The second fraction gave a red-purple solid (2.6 g) which was crystallized (ethanol) to give 1-p-toluidino-5-chloroanthraquinone (LXI) (2.3 g, 37%) as dark red needles, m.p. 165-166°. (calcd. for $C_{21}H_{14}NO_2Cl$: C, 72.52; H, 4.06; N, 4.03. Found: C, 71.82; H, 3.97; N, 3.74.); mass spectrum

m/e 349 (M^+ ^{37}Cl) (32), 348 (M^+ ^{13}C) (26), 347 (M^+) (100%), 332 ($M-CH_3$) (3), 254 ($M-CH_3-C_6H_6$) (4), 241 ($M-NHC_6H_4CH_3$) (5), 240 ($M-NHC_6H_4CH_3-H$) (4), 173.5 (M^{++}) (10), 166 $(M-CH_3)^{++}$ (8); ν_{max} 1675 (s), 1625 (s), 1590, 1570, 1520 (br), 1380 (w), 1355 (w), 1315, 1255 (s), 1190, 1165, 1130, 800 (sh), 750 (sh), 745 (sh), 700 (sh), 695 (sh) cm^{-1}; ^1H-nmr ($CDCl_3$) 8.2 (br s, 1H), 7.7-7.3 (m, 6H), 7.2 (s, 4H), 2.4 (s, 3H).

(ii) Dehydration of 1,5-bis(p-toluidino)-anthraquinone (LXII)

1,5-Bis(p-toluidino)-anthraquinone (0.5 g, 0.0012 mole) was added to 70% aqueous H_2SO_4 (30 ml) and refluxed for 30 minutes. The resulting deep blue solution was allowed to cool, poured into water (300 ml) and neutralized with aqueous NaOH. The solution was then extracted with chloroform (4 x 100 ml) and the extracts dried (Na_2SO_4) and the solvent evaporated to give a purplish-red solid (0.5 g). Crystallization (ethanol) gave the diacridine (LXIII) (0.4 g, 83%) as purple-red crystals, m.p. >320° (lit.[102] m.p. not available); mass spectrum m/e 383 (M^+ ^{13}C) (36), 382 (M^+) (100%), 367 ($M-CH_3$) (9), 191 (M^{++}) (13), 179.5 $(M-CH_3)^{++}$ (6); I.R. shows no carbonyl stretch; ^1H-nmr ($CDCl_3$) 8.4-7.7 (m, 10H), 7.3 (s, 2H), 2.6 (s, 6H).

(iii) Dehydration of 1-p-toluidino-5-chloroanthraquinone (LXI)

1-p-Toluidino-5-chloroanthraquinone (2.0 g, 0.0058 mole) was heated in 70% aqueous H_2SO_4 (50 ml) at 160-180° for 1 hour. The mixture was allowed to cool, diluted with water (250 ml) and basified with aqueous NaOH. The resulting solid was collected by suction filtration. This

chocolate-brown material (1.92 g) was chromatographed to give the acridine (LXIV) (1.1 g, 58%) which was used without further purification in the next reaction. An analytical sample crystallized from ethanol as golden-brown needles, m.p. 218-221° (Calcd. for $C_{21}H_{12}NOCl$: C, 76.48; H, 3.67; N, 4.25; Cl, 10.75. Found: C, 76.34; H, 3.68; N, 4.30; Cl, 10.43.); mass spectrum m/e 331 (M^+ ^{37}Cl) (34), 330 (M^+ ^{13}C) (25), 329 (M^+) (100%), 301 (M-CO) (5), 295 (M + 1 -Cl) (39), 266 (11), 265 (M-CO-HCl) (14), 264 (265-H) (16), 165.5 $(M + 2)^{++}$ (3), 164.5 (M^{++}) (8), 132.5 $(M-CO-HCl)^{++}$ (39); ν_{max} 1663 (s), 1575 (sh), 1515 (sh), 1430 (w), 1405 (sh), 1287, 1270, 860 (sh), 797 (s, sh), 730, 700 (sh) cm^{-1}; ^1H-nmr ($CDCl_3$) 8.5-7.3 (m, 9H), 2.6 (s, 3H).

(iv) Attempted cleavage of the acridine (LXIV)

The acridine (LXIV) (0.75 g, 0.0023 g) was added to the mixture made by adding water (0.12 g, 0.0068 mole) to a stirred suspension of potassium t-butoxide (2.6 g, 0.023 mole) in monoglyme (1,2-dimethoxyethane) (50 ml). The reaction mixture was kept under dry nitrogen. After addition, the mixture was refluxed for 1 hour and then allowed to cool.

The resulting solution was diluted with water (300 ml) and extracted with ether (3 x 50 ml). The ether solution was then washed (H_2O), dried (Na_2SO_4) and evaporated to give a trace of a brownish residue which was not further investigated.

The aqueous layer was carefully acidified (concentrated HCl) and extracted with ether (10 x 50 ml). The combined extracts were washed

with saturated aqueous potassium bicarbonate (4 x 100 ml), then with water and then dried; evaporation of the solvent gave a reddish-brown mixture (0.04 g) which was not further investigated.

The combined bicarbonate washings were cautiously acidified (concentrated HCl) and extracted with ether (5 x 50 ml). The ethereal solution was washed, dried and the solvent was evaporated to give a yellow-brown acidic fraction (0.07 g). T.l.c. indicated that it was a complex mixture which could not be readily resolved. The mass spectrum did not indicate any of the desired acridine-carboxylic acid (m/e 347).

The acidified aqueous phase was filtered and the resultant residue extracted with chloroform. Evaporation of the solvent gave a blackish residue (0.25 g). Considerable chloroform insoluble material remained. The mass spectrum showed a major peak at m/e 311 but not at m/e 347.

Reaction of 1,5-dichloroanthraquinone with potassium hydroxide

(i) 1,5-Dichloroanthraquinone (3.45 g, 0.0125 mole) together with KOH (3.5 g, 0.0625 mole) was refluxed in cellosolve (2-ethoxyethanol) (50 ml) for 2 hours. Upon cooling, the mixture was filtered to give a light brown solid (2.4 g) and a dark red filtrate.

The solid material, after being crystallized three times from chloroform/acetone (charcoal) gave what is identified as 1,5-di(2-ethoxy-ethoxy)anthraquinone (XLIX) (1.7 g, 35%) as light yellow needles, m.p. 132°. (Calcd. for $C_{22}H_{24}O_6$: C, 68.73; H, 6.29. Found: C, 68.63; H, 6.22.); mass spectrum m/e 384 (M^+) (18), 339 ($M-C_2H_5O$) (37), 325 ($M-C_2H_5OCH_2$) (11), 312 ($M-C_2H_5OCH=CH_2$) (5), 293 ($M-C_2H_5O-C_2H_5OH$) (15), 266 ($M-C_2H_5OCH=CH_2-C_2H_5OH$) (41), 253 ($M-C_2H_5OCH=CH_2-C_2H_5OCH_2$) (91), 240 ($M-2C_2H_5OCH=CH_2$) (100%), 238 ($266-C_2H_4$) (74), 224 (17), 210 (6), 208 (6), 195 (7), 184 (5), 168 (5), 150 (11), 139 (25); ν_{max} 2960, 2930, 2860 (s), 1665 (s), 1590 (s), 1485 (sh), 1475 (sh), 1460, 1445 (s, sh), 1420 (sh), 1380 (sh), 1330, 1320, 1280 (br), 1255 (s, br), 1180 (sh), 1140, 1125 (br), 1075 (sh), 990, 885, 845, 800, 765 (sh), 710 (s, sh) cm^{-1}; ^1H-nmr ($CDCl_3$) 8.1-7.2 (m, 6H), 4.4 (skewed triplet, J = 5.4 Hz, 4H), 4.0 (skewed triplet, J = 5.4 Hz, 4H), 3.7 (q, J = 7.0 Hz, 4H), 1.3 (t, J = 7.0 Hz, 6H).

The previously obtained red filtrate was diluted with water (200 ml), filtered and then acidified (concentrated H_2SO_4). Filtration gave a golden brown solid (0.97 g). Chromatography (benzene, chloroform) followed by crystallization (ethanol) afforded 1-(2-ethoxy-ethoxy)-5-hydroxyanthraquinone (L) (0.7 g, 18%) as bright yellow microcrystals,

m.p. 98-100°. (Calcd. for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found: C, 68.72; H, 5.02.); mass spectrum m/e 312 (M^+) (5), 266 ($M-C_2H_5OH$) (25), 253 ($M-C_2H_5OCH_2$) (50), 240 ($M-C_2H_5OCH=CH_2$) (100%), 224 ($M-C_2H_5OCH=CHOH$) (18), 212 (240-CO) (6), 196 (224-CO) (6), 184 (240-2CO) (10), 168 (8), 155 (13), 139 (55); ν_{max} 2950, 2850 (br), 1665 (s), 1620 (s), 1580 (br), 1445 (s, br), 1360, 1285 (br), 1255 (s, br), 1175, 1140, 1110, 1070, 1060, 1015 (sh), 940, 880 (sh), 855 (sh), 800 (sh), 775 (s), 700 (s, sh) cm^{-1}; ^1H-nmr ($CDCl_3$) 12.6 (singlet, 1H), 8.2-7.1 (multiplet, 6H), 4.3 (skewed triplet, J = 5.4 Hz, 2H), 3.9 (skewed triplet, J = 5.4 Hz, 2H), 3.7 (quartet, J = 7.0 Hz, 2H), 1.3 (triplet, J = 7.0 Hz, 3H).

(ii) The reaction was repeated with 1,5-dichloroanthraquinone (3.45 g, 0.0125 mole) in DMSO (50 ml) and slowly adding a solution of KOH (2.1 g, 0.0375 mole) in water (10 ml). The mixture was refluxed for 30 minutes, cooled and diluted with water (300 ml). Careful acidification with concentrated H_2SO_4 gave a precipitate which was collected by suction filtration, washed with water and air-dried. The result was a yellowish-green solid (3.2 g) which, by the mass spectrum, was found to contain some 1,5-dichloroanthraquinone (m/e 276) as well as 1-hydroxy-5-chloroanthraquinone (m/e 258) and 1,5-dihydroxyanthraquinone (m/e 240). This mixture could not be separated by physical or chromatographic methods and was not further studied.

Preparation of 1-hydroxy-5-chloroanthraquinone (LI)

The method of Green[66] was followed. 1-Amino-5-chloroanthraquinone (2.0 g, 0.008 mole) in concentrated H_2SO_4 (20 ml) was treated at 0° with $NaNO_2$ (0.6 g, 0.0045 mole) during one hour and stirring continued for 8 hours. The mixture was then heated at 130-140° for 5 minutes and then poured into cold water (250 ml). The resulting suspension was boiled and filtered to give a yellowish-brown solid (0.95 g). This was dissolved in 2% NaOH (aqueous) and the solution filtered to give a brownish solid and a red filtrate. The solid was identified as 1-amino-5-chloroanthraquinone (0.9 g, 45%); its mass spectrum and R_f were identical with those of the starting material, although it was slightly impure (t.l.c.). It was not further purified.

The red filtrate was carefully acidified with concentrated HCl and yielded a yellowish precipitate. Chromatography afforded 1-hydroxy-5-chloroanthraquinone (LI) (0.4 g, 19%) as bright yellow needles (ethanol), m.p. 222-224° (lit.[66] 221-222°; 223-224°); mass spectrum m/e 260 (M^+ ^{37}Cl) (34), 258 (M^+) (100%), 257 (M-H) (12), 230 (M-CO) (14), 224 (M + 1 -Cl) (94), 202 (M-2CO) (18), 196 (224-CO) (10), 173 (M-2CO-HCO) (5), 168 (M + 1 -2CO-Cl) (17), 139 ($C_{11}H_7^+$) (38); ν_{max} 1670 (s, sh), 1630 (s), 1575, 1445, 1360 (s, br), 1320, 1305, 1260 (s, br), 1185, 1150, 1030 (sh), 875, 830, 810 (s, sh), 760 (s, sh), 730, 695 (s, sh) cm^{-1}; ^1H-nmr ($CDCl_3$) 11.6 (s, 1H), 8.4-7.3 (m, 6H).

Reaction of 1-hydroxy-5-chloroanthraquinone with potassium amide in liquid ammonia

To a stirred mixture of potassium amide in redistilled liquid ammonia (made from potassium (1.6 g, 0.04 atom) in 300 ml liquid ammonia) was added a solution of 1-hydroxy-5-chloroanthraquinone (0.55 g, 0.002 mole) in dry tetrahydrofuran (50 ml). The reaction mixture was stirred for 6 hours followed by careful addition of ammonium chloride (3.0 g) and ether (50 ml). The ammonia was allowed to evaporate overnight.

The residual material was treated with 2N hydrochloric acid (200 ml) and this was extracted with ether (4 x 50 ml). The ether solution was washed with saturated aqueous potassium bicarbonate (3 x 50 ml). Acidification (concentrated H_2SO_4) of these washings produced no solid. The ether solution was then extracted with 40% (w/v) sodium hydroxide solution (2 x 50 ml) to give a red aqueous solution. This solution was acidified (concentrated H_2SO_4) and extracted with chloroform (3 x 50 ml). The chloroform solution was washed (H_2O), dried (Na_2SO_4) and the solvent evaporated to give 1-hydroxy-5-chloroanthraquinone (0.5 g, 91%) as golden yellow needles which were identical (m.p., R_f and mass spectrum) with the starting material. No other products were observed.

Reaction of 1-hydroxy-5-chloroanthraquinone with potassium t-butoxide in t-butylbenzene

A mixture of 1-hydroxy-5-chloroanthraquinone (0.5 g, 0.002 mole) and potassium t-butoxide (0.7 g, 0.006 mole) (made from 0.25 g potassium in t-butanol) in t-butylbenzene (25 ml) was refluxed for

12 hours. The hot mixture was then poured into an evaporating dish and the solvent allowed to evaporate overnight. The resulting black residue was taken up in water (150 ml) and the aqueous solution A extracted with chloroform (3 x 50 ml).

The chloroform solution was washed and dried and the solvent removed to give an orange-brown solid (0.1 g). Chromatography of this material returned some 1-hydroxy-5-chloroanthraquinone (0.01 g, 2%); the mass spectrum was identical with that of the starting material. Some bright red material was retained by the column and could not be eluted.

The aqueous solution A was acidified with concentrated H_2SO_4 and the solution was then extracted with chloroform (3 x 50 ml). The chloroform solution was washed with saturated aqueous potassium bicarbonate (4 x 50 ml). Acidification of the latter produced no solid. The chloroform solution was then extracted with 10% (w/v) sodium hydroxide solution (2 x 50 ml) to give a purple aqueous solution. Evaporation of the remaining chloroform solution gave a negligible amount of tarry material.

The purple aqueous solution was carefully acidified (concentrated H_2SO_4) and then extracted with chloroform (3 x 50 ml) and this was washed and dried and the solvent was evaporated. A brownish-yellow solid (0.2 g) resulted. Chromatography afforded what is identified as 1-hydroxy-anthraquinone (LV) (0.02 g, 5%) as yellow crystals, m.p. 181-185° (lit.[103] 193°); mass spectrum m/e 225 (M^+ ^{13}C) (15), 224 (M^+) (100%), 223 (M-H) (30), 196 (M-CO) (12), 168 (M-2CO) (20), 139 (M-2CO-HCO) (35); metastable observed at m/e 171.5, assigned to

$[M^+] \longrightarrow [M-CO]^+ + CO$ (m^*_{obs}: m/e 171.5; m^*_{calc}: m/e 171.5); metastable observed at m/e 144, assigned to $[M-CO]^+ \longrightarrow [M-2CO]^+ + CO$ (m^*_{obs}: m/e 144; m^*_{calcd}: m/e 144); ν_{max} 2910, 2840 (w), 1740, 1665, 1587 (sh), 1450 (s, br), 1360, 1350, 1287 (sh), 1255 (br), 1225, 1150, 875 (sh), 860 (sh), 825, 760 (br), 695 (s, sh) cm^{-1}; ^1H-nmr ($CDCl_3$) 11.4 (s, 1H), 8.4-7.3 (m, 7H). The mass spectrum was identical with that of an authentic sample of 1-hydroxyanthraquinone.

Attempted preparation of 1-mercapto-5-chloroanthraquinone (LVII)

1-Amino-5-chloroanthraquinone (1.5 g, 0.0058 mole) was dissolved in 60% H_2SO_4 (20 ml) and maintained at 0°. $NaNO_2$ (0.46 g, 0.0064 mole) was added in portions to the stirred solution over 30 minutes. The suspension was then allowed to warm to room temperature to give a clear yellow solution. This solution was added dropwise to a stirred mixture of sodium sulfhydrate (0.6 g, 0.0065 mole) and copper powder (0.5 g) in water (35 ml) at 60-70°, so as to maintain a brownish coloured reaction mixture. After addition the stirred mixture was kept at 60-70° for an additional hour. It was then filtered and the filtrate was extracted with chloroform (3 x 50 ml). The chloroform solution was extracted with 5% (w/v) sodium hydroxide (2 x 50 ml), washed (H_2O), dried (Na_2SO_4) and the solvent evaporated. This gave impure 1-amino-5-chloro-anthraquinone (0.9 g, 60%) as a reddish-brown solid; its R_f and mass spectrum were identical with those of the starting material and it was not purified.

The sodium hydroxide washings were combined and acidified (concentrated H_2SO_4) and then extracted with chloroform. Evaporation of the solvent gave a yellowish brown solid (0.2 g) which was found to contain sulfur (S_8, m/e 256) and an unidentified compound (m/e 254).

Reaction of anthraquinones with sodium azide

1,5-Dichloroanthraquinone

To a stirred solution of 1,5-dichloroanthraquinone (8.5 g, 0.03 mole) in concentrated H_2SO_4 (75 ml) was added NaN_3 (6.0 g, 0.09 mole) in portions so as to maintain a reaction temperature of 40-50° (about 0.5 hour). After addition was completed the reaction mixture was stirred for an additional 3.5 hours at 40-50°. The mixture was then slowly poured into water (250 ml) with stirring, filtered and the residue washed with water and a small amount of acetone and then dried. This gave a creamy-white powder (8.78 g) which was found to be a mixture of two components (t.l.c.) which were isomeric (mass spectrum).

On the basis of the spectral data, these were tentatively identified as two lactams M and N; mass spectrum m/e 293 (M^+ ^{37}Cl) (58), 292 (M - 1, ^{37}Cl) (61), 291 (M^+) (83), 290 (M-H) (70), 263 (M-CO) (100%), 256 (M-Cl) (88), 235 (M-2CO) (43), 228 (M-Cl-CO) (18), 200 (M=Cl-2CO) (72), 173 (200-HCN) (23), 164 (200-HCl) (78), 149 (42); ν_{max} 3175, 3070, 3045, 2955, 2895 (w), 1695 (s) (C=O), 1660 (br, s) (C=O lactam), 1590 (sh), 1575, 1450 (br, s), 1375 (br, s), 1280 (s), 1245, 1200 (sh), 1190 (sh), 1130, 840 (br), 820 (sh), 810 (sh, s), 790 (sh), 775 (sh), 720 (sh, s), 705 (sh), 660 (sh) cm^{-1}.

(ii) The mixture from the previous reaction (8.78 g) was suspended in a solution of KOH (2.0 g, 0.036 mole) in 95% ethanol (100 ml) and heated to boiling. The resulting orange-yellow solution was cooled and filtered

and then poured into water (150 ml). This was filtered to give an off-white solid A (4.1 g) and a yellow filtrate B. Filtrate B was carefully acidified with concentrated H_2SO_4 to give a brownish gum. The gum was allowed to settle, the supernatant decanted and the gum then taken up in the minimum amount of ethanol (35 ml). This was filtered to give an off-white solid C (0.5 g) and a yellow filtrate D. Solids A and C were found to be identical (the lower R_f component of the mixture, by t.l.c.) and were combined. Filtrate D was poured into water (100 ml) and the resulting precipitate collected by suction filtration as a yellow solid (3.4 g). This was crystallized from ethanol/water to give the amino-carboxylic acid P (3.2 g, 35%) as yellow spikes, m.p. 182-184° (Calcd. for $C_{14}H_9NO_3Cl_2$: C, 54.22; H, 2.92; Cl, 22.86. Found: C, 54.13; H, 2.96; Cl, 23.07.); mass spectrum m/e 311 (M^+ ^{37}Cl) (58), 309 (M^+) (100%), 291 (M-H_2O) (16), 290 (M-H_2O-H) (20), 274 (M-Cl) (30), 263 (M-H_2O-CO) (62), 256 (M-H_2O-Cl) (73), 236 (263-HCN) (18), 228 (256-CO) (32), 200 (256-2CO) (21), 183 ($C_{12}H_4Cl^+$) (24), 164 (21), 154 ($C_7H_5NOCl^+$) (67), 139 (12), 126 (154-CO) (33); ν_{max} 3450 (s) (-OH), 3340, 2900 (br), 2550 (br), 1680 (br), 1640, 1615, 1575 (br), 1530 (sh), 1460, 1440, 1410, 1300 (br, s), 1240 (br, s), 1145, 1075, 935 (br, w), 865, 815, 795 (sh), 755 (s), 740 (s), 730 (s), 715 (sh, s), 655 (s) cm^{-1}.

The combined solids A, C gave the lactam M (4.2 g, 48%) as off-white prisms (ethanol), m.p. 321-322°; Calcd. for $C_{14}H_7NO_2Cl_2$: C, 57.56; H, 2.42; Cl, 24.27. Found: C, 57.63; H, 2.38; Cl, 24.05); mass spectrum m/e 293 (M^+ ^{37}Cl) (53), 292 (M - 1, ^{37}Cl) (57), 291 (M^+) (84), 290 (M-H) (82), 263 (M-CO) (100%), 256 (M-Cl) (88), 235 (M-2CO) (62),

200 (M-2CO-Cl) (88), 173 (200-HCN) (33), 164 (200-HCl) (85); ^{1}H-nmr (d_6-DMSO) 11.3 (br s, 1H), 7.9-7.1 (m, 6H).

(iii) The yellow amino-carboxylic acid P (1.6 g, 0.0052 mole) was added to a mixture made by adding water (0.28 g, 0.016 mole) to a rapidly stirred solution of potassium t-butoxide (5.8 g, 0.052 mole) in 1,2-dimethoxyethane (50 ml) under nitrogen. The mixture was stirred at 20° for 3 hours and then poured into water (250 ml). The solution was extracted with ether (extracts discarded), acidified (concentrated H_2SO_4) and again extracted with ether (3 x 50 ml). The combined extracts were washed with saturated aqueous potassium bicarbonate (2 x 50 ml). The bicarbonate washings were carefully acidified (concentrated HCl) and extracted with ether (2 x 50 ml). The ether solution was washed with water, dried (Na_2SO_4) and the solvent evaporated to give a light yellow residue (1.3 g). This mixture was esterified by refluxing in methanol (25 ml) plus concentrated H_2SO_4 (2 ml) for 3 hours. The mixture was then poured into water and extracted with ether. The ether was washed with saturated aqueous potassium bicarbonate (to remove any unreacted acid), then with water and dried with Na_2SO_4.

The ethereal solution was then concentrated and the residue analyzed by g.l.c.* This showed the presence of the methyl ester of 3-chlorobenzoic acid (by comparison with an authentic sample). Thus, acid P is

---

* Done on F & M Laboratory Chromatograph Model 700 with column temperature of 150°, flow rate = 40 ml/min and using a 6 foot column of diethylene glycol succinate (DEGS) on chromosorb (80-100 mesh).

identified as 3,6'-dichloro-2-amino-benzophenone-2'-carboxylic acid (LXXXI) and compound N as its lactam. By deduction, compound M must then be the lactam of 3,6'-dichloro-2'-amino-benzophenone-2-carboxylic acid (LXXXII).

1,8-Dichloroanthraquinone

1,8-Dichloroanthraquinone (2.76 g, 0.01 mole) was reacted as previously with NaN_3 (1.95 g, 0.03 mole) in concentrated H_2SO_4 (35 ml) for 4 hours at 40-50°. Work-up with water followed by filtration, washing with water and a small amount of acetone and drying gave a yellowish white solid (2.3 g) which contained two isomeric components (t.l.c., mass spectrum).

The mixture was heated to boiling in 2% ethanolic KOH solution (25 ml) and the solution was then filtered and diluted with water (100 ml). The resulting precipitate was collected and dried to give an off-white solid (0.5 g) which contained one component only (t.l.c.). Crystallization from ethanol (carbon) gave (by analogy) the lactam of 3,3'-dichloro-2-aminobenzophenone-2'-carboxylic acid (LXXXV) (0.41 g, 14%) as pale yellowish-white prisms, m.p. 313-315°; (Calcd. for $C_{14}H_7NO_2Cl_2$: C, 57.56; H, 2.42; N, 4.80. Found: C, 57.51; H, 2.47; N, 4.83.); mass spectrum m/e 293 (M^+ ^{37}Cl) (60), 292 (M - 1, ^{37}Cl) (48), 291 (M^+) (100%), 290 (M-H) (53), 263 (M-CO) (93), 256 (M-Cl) (81), 235 (M-2CO) (24), 228 (M-Cl-CO) (14), 200 (M-Cl-2CO) (41), 173 (200-HCN) (16), 164 (200-HCl) (43); ν_{max} 3000 (br, s), 1650 (br, s), 1570 (br, s), 1445 (s), 1350 (br, s), 1250, 1200, 1110, 970, 920 (sh), 835 (s), 815 (s), 795, 770 (s), 700, 665 cm^{-1}; ^1H-nmr (d_6-DMSO) 11.2 (br s, 1H), 8.0-7.0 (m, 6H).

The filtrate was carefully acidified (concentrated H_2SO_4) with stirring after which it became an opaque yellow colour. On standing, a brownish yellow gum separated. The supernatant was decanted and the gum taken up in ethanol (20 ml) and then filtered. After repeated attempts at crystallization from ethanol/water (carbon), 2,2'-dichloro-6-aminobenzophenone-6'-carboxylic acid (LXXXVII) (1.1 g, 36%) was obtained as bright yellow crystals, m.p. 170-172°; (Calcd. for $C_{14}H_9NO_3Cl_2$: C, 54.22; H, 2.92; N, 4.52; Cl, 22.86. Found: C, 54.37; H, 2.94; N, 4.45; Cl, 23.09.); mass spectrum m/e 311 (M^+ ^{37}Cl) (68), 209 (M^+) (81), 290 (M-H_2O-H) (88), 265 (M-CO_2) (94), 263 (M-HCO_2H) (100%), 256 (M-H_2O-Cl) (75), 235 (M-HCO_2H-CO) (26), 230 (M-CO_2-Cl) (38), 200 (235-Cl) (31), 183 ($C_8H_4ClO_3^+$) (28), 164 (200-HCl) (54), 154 ($C_7H_5NOCl^+$) (88), 139 (183-CO_2) (33), 126 (154-CO) (39), 111 ($C_6H_4Cl^+$) (50), 99 (126-HCN) (48); ν_{max} 3470, 3340, 2940 (br), 2640 (w), 1700 (br, s), 1635, 1610, 1575 (br), 1535, 1445 (br), 1400, 1320, 1300, 1275, 1250, 1210 (sh), 1150, 1080, 845 (sh), 820, 800, 780 (sh), 745 (sh), 725 (sh), 700, 665, 635 cm^{-1}.

1-Chloroanthraquinone

1-Chloroanthraquinone (2.42 g, 0.01 mole) was reacted with NaN_3 (1.95 g, 0.03 mole) in concentrated H_2SO_4 (35 ml) for 4 hours at 40-50°. Standard work-up with water and filtration gave a pinkish white solid (2.33 g) which contained two isomeric components (t.l.c., mass spectrum). The mixture was heated in ethanolic KOH, as previously, until it dissolved and then the solution was filtered and poured into water. Filtration gave a brownish-white solid (1.03 g) and an ethanolic solution.

After crystallization from DMSO/water (carbon) the solid gave (by analogy with the previous cases) the lactam of 3-chloro-2'-amino-benzophenone-2-carboxylic acid (LXXXVIII) (0.75 g, 29%) as white needles, m.p. 223-225°. (Calcd. for $C_{14}H_8NO_2Cl$: C, 65.26; H, 3.13; N, 5.44; Cl, 13.76. Found: C, 65.21; H, 3.14; N, 5.54; Cl, 13.80.); mass spectrum m/e 259 (M^+ ^{37}Cl) (33), 258 (M - 1, ^{37}Cl) (45), 257 (M^+) (90), 256 (M-H) (100%), 229 (M-CO) (70), 222 (M-Cl) (33), 201 (M-2CO) (38), 194 (M-Cl-CO) (8), 166 (M-2CO-Cl) (45), 139 (166-HCN) (23); ν_{max} 3180, 3045, 2960 (w), 1670 (s), 1655 (s), 1610, 1580, 1485 (sh), 1450, 1435, 1375 (br), 1330, 1290, 1235, 835 (br), 805 (sh), 780 (sh), 762 (sh), 745, 725 (w), 697 (sh) cm^{-1}; ^1H-nmr ($CDCl_3$) 9.3 (br s, 1H), 7.8-7.2 (m, 7H).

The ethanolic solution was carefully acidified with concentrated H_2SO_4 after which a dark yellow oil precipitated. After decanting the supernatant liquid, the oil was taken up in cold ethanol (20 ml) and this solution was filtered and the solvent evaporated. The resultant gum gave, after numerous crystallizations from ethanol/water (carbon), 3-chloro-3-aminobenzophenone-2'-carboxylic acid (LXXXIX) (0.65 g, 24%) as pale orange-yellow plates, m.p. 155-159° (lit.[76] m.p. not available); (Calcd. for $C_{14}H_{10}NO_3Cl$: C, 60.99; H, 3.66; N, 5.08; Cl, 12.86. Found: C, 60.96; H, 3.83; N, 5.01; Cl, 12.79.); mass spectrum m/e 277 (M^+ ^{37}Cl) (32), 275 (M^+) (100%), 256 ($M-H_2O-H$) (84), 247 (M-CO) (5), 240 (M-Cl) (3), 230 ($M-CO_2H$) (66), 222 ($M-H_2O-Cl$) (11), 201 ($M-CO_2H-HCO$) (19), 194 (222-CO) (13), 166 (194-CO) (17), 154 ($C_7H_5NOCl^+$) (45), 149 ($C_8H_5O_3^+$) (28), 139 (166-HCN) (15), 126 (154-CO) (15), 120 ($C_6H_4CO_2^+$) (14); ν_{max} 3460, 3340, 2900 (br), 1680 (br, s), 1640, 1605, 1575, 1535, 1480, 1435 (br), 1287 (br, s), 1245 (s), 1137, 1080, 930, 800, 765, 745, 715 (sh) cm^{-1}.

2-Chloroanthraquinone

2-Chloroanthraquinone (1.5 g, 0.0062 mole) was treated with NaN_3 (1.2 g, 0.018 mole) in concentrated H_2SO_4 (15 ml) as previously. Standard work-up gave a brownish-white powder (1.34 g) which could be crystallized from DMSO/water as white needles (1.1 g). T.l.c. indicated that this was a mixture of at least two components with almost identical R_f values. No starting material was observed. The mass spectrum suggested a mixture of isomeric lactams (M^+ m/e 257); mass spectrum m/e 259 (M^+ ^{37}Cl) (29), 258 (M - 1, ^{37}Cl) (58), 257 (M^+) (71), 256 (M-H) (100%), 229 (M-CO) (42), 222 (M-Cl) (19), 201 (M-2CO) (13), 166 (M-2CO-Cl) (25), 139 (M-2CO-Cl-HCN) (20); ν_{max} 3180, 3040, 2960, 1675 (s) (C=O), 1665 (s) (C=O lactam), 1655 (s) (C=O lactam), 1585, 1480, 1440, 1412, 1375, 1325, 1235, 837 (br). The mixture could not be separated by preferential hydrolysis but gave a mixture of acids (t.l.c.). It was not separated or investigated further.

Anthraquinone

Anthraquinone (1.3 g, 0.006 mole) was treated similarly with NaN_3 (1.2 g, 0.018 mole) in concentrated H_2SO_4 (15 ml). Standard work-up gave a white powder (1.32 g). Crystallization from DMSO/water gave the lactam of 2-amino-benzophenone-2'-carboxylic acid (LXVIII) (1.1 g, 82%) as pure white needles, m.p. 250-251° (lit.[74,75] 245°); (Calcd. for $C_{14}H_9NO_2$: C, 75.34; H, 4.04; N, 6.28. Found: C, 75.20; H, 3.95; N, 6.27.); mass spectrum m/e 224 (M^+ ^{13}C) (16), 223 (M^+) (88), 222 (M-H) (100%), 195 (M-CO) (67), 167 (M-2CO) (44), 140 (M-2CO-HCN) (9); ν_{max} 3170 (w), 3030 (br), 1660 (s) (C=O), 1645 (s) (C=O lactam),

1590, 1560, 1530 (N-H cyclic), 1505, 1480 (sh), 1430 (sh), 1390 (br), 1305 (sh), 1230 (br), 1155 (sh), 875 (br), 845 (br), 795 (sh), 780 (sh), 760 (s), 725 (sh, s), 700 (s), 675 cm^{-1}.

Anthrone

Anthrone (1.2 g, 0.006 mole) was reacted with NaN_3 (1.2 g, 0.018 mole) as above. Standard work-up of the resulting reaction mixture gave a light yellow powder (1.13 g). This was found to be unchanged anthrone; it was identical with the starting material (R_f and mass spectrum).

Attempted Decarbonylation of an Azepindione to an Acridone

(i) The lactam of 2-amino-3'-chlorobenzophenone-2'-carboxylic acid (1.0 g, 0.004 mole) and KF (5.0 g, 0.086 mole) were stirred in refluxing DMSO (30 ml) for 4 hours in a flask with a reflux condenser fitted with a drying tube ($CaCl_2$). The mixture was then added to water (200 ml) and the resulting precipitate collected by suction filtration, washed with water and dried. This gave a light brown powder (0.8 g) which was found to be a mixture (t.l.c.). Although this mixture was not separated and purified it was found to contain some starting material (m/e 257) and what was tentatively identified as 2-amino-3'chloro-benzophenone (XCIX, X = H) (m/e 231 (M^+), 230 (M-H), 196 (M-Cl)). The latter could not be obtained in pure form by crystallization (ethanol/water) and chromatography was not attempted.

(ii) A stirred suspension of the lactam of 2-amino-3,6'-dichloro-benzophenone-2'-carboxylic acid (1.0 g, 0.0034 mole) and KF (10.0 g, 0.17 mole) in DMSO (30 ml) was heated to reflux for 12 hours. The resulting mixture was poured into cold water (200 ml) and filtered. This gave a yellowish brown solid (0.8 g) which contained mainly starting material (m/e 291) and a new compound, as well as some tarry material (t.l.c.). The mixture could not be purified by crystallization (ethanol/water) and chromatography was not attempted. However, on the basis of the mass spectral data, the new compound was tentatively identified as 2-amino-3',6-dichlorobenzophenone (XCIX, X = Cl) (m/e 265 (M^+), 264 (M-H), 230 (M-Cl)).

The reaction of chloroanthraquinones with hexamethylphosphoramide (HMPA)

1-Chloroanthraquinone

1-Chloroanthraquinone (2.42 g, 0.01 mole) was refluxed in HMPA (20 ml) for 15 minutes. The reaction mixture was then allowed to cool to room temperature and poured into cold water (150 ml). The resulting precipitate was collected by suction filtration and allowed to air-dry, yielding a dark red solid (2.32 g). This was chromatographed to give three fractions.

Fraction 1 gave, on evaporation, 1-chloroanthraquinone (0.22 g, 9%) as a yellow solid, m.p. 158-160°; R_f, mass spectrum and m.p. were identical with those of the starting material. Fraction 2 gave, on evaporation and crystallization (ethanol), 1-methylaminoanthraquinone (0.70 g, 30%) as red micro-crystals with a golden lustre, m.p. 172-173° (lit.[104], 167° (170°)); mass spectrum m/e 237 (M^+) (100%), 236 (37), 220 (67), 209 (15), 208 (15), 180 (24), 165 (17), 164 (11), 163 (6), 152 (29), 151 (19), 150 (11), 149 (17), 129 (57); ν_{max} 3325 (sh), 2925 (w, br), 1680 (sh), 1640 (sh), 1600 (sh), 1520, 1405, 1368, 1317 (s), 1280 (s), 1185, 1075, 990 (sh), 815, 740, 715 (sh) cm^{-1}; ^{1}H-nmr ($CDCl_3$) 9.5 (br s, 1H), 8.5-6.8 (m, 7H), 3.0 (d, J = 4.9 Hz, 3H); ^{1}H-nmr ($CDCl_3$ + D_2O) 8.5-6.8 (m, 7H), 3.0 (s, 3H). Fraction 3 gave, on evaporation and crystallization (ethanol), 1-dimethylaminoanthraquinone (0.05 g, 2%) as dark red prisms, m.p. 139-140° (lit.[105], 140-141°); mass spectrum m/e 251 (M^+) (82), 250 (12), 236 (83), 234 (100%), 222 (15), 220 (13), 219 (11), 209 (7), 208 (6), 193 (4), 180 (9), 165 (17), 152

(18), 151 (13), 150 (7), 139 (2), 125.5 (M^{++}) (3); ν_{max} 2920 (w, br), 1650 (s), 1635, 1575, 1495 (sh), 1420 (sh), 1365, 1310, 1260 (s), 1205, 1175, 1070, 1060, 1015, 925 (sh), 795 (sh), 705 (s) cm^{-1}; ^{1}H-nmr ($CDCl_3$) 8.3-7.2 (m, 7H), 3.0 (s, 6H).

2-Chloroanthraquinone

2-Chloroanthraquinone (2.42 g, 0.01 mole) was refluxed in HMPA (20 ml) for 45 minutes. The reaction mixture was treated as in the previous reaction and yielded a brick-red residue (2.94 g). Chromatography gave three fractions.

Fraction 1, on evaporation, gave 2-chloroanthraquinone (0.77 g, 32%) as pale yellow needles, m.p. 209-211°; R_f, mass spectrum and m.p. were identical with those of the starting material. Fraction 2, on evaporation, gave a red mixture (0.03 g) which was rechromatographed on a micro-column to give 2-methylaminoanthraquinone (0.008 g, 0.3 %) as a bright red solid, m.p. 149-155° (lit.[106], 226-227°); it was found to be contaminated with a trace of 2-chloroanthraquinone and another impurity with M^+ at m/e 281/279 (the isotopic ratio indicated the presence of one chlorine); mass spectrum m/e 237 (M^+) (100%), 236 (33), 220 (85), 209 (9), 208 (9), 192 (4), 180 (14), 167 (10), 165 (9), 152 (15), 149 (34), 139 (4), 118.5 (M^{++}) (7); ν_{max} 3450 (br), 2925, 1725, 1675, 1627 (sh), 1595, 1515, 1255 (s, br), 1180 (sh), 1070 (sh), 985 (sh), 733 (sh), 705 (s, sh) cm^{-1}; ^{1}H-nmr ($CDCl_3$) 9.7 (br s, 1H), 8.5-7.0 (m, 7H), 3.1 (d, J = 4.9 Hz, 3H); ^{1}H-nmr ($CDCl_3$ + D_2O) 8.5-7.0 (m, 7H), 3.1 (s, 3H).

Fraction 3 afforded, after crystallization (ethanol), 2-dimethylaminoanthraquinone (0.91 g, 36%) as bright orange needles, m.p. 186-187°

(lit.[105], 188-189°); mass spectrum m/e 251 (M^+) (100%), 250 (89), 236 (5), 235 (3), 234 (3), 222 (2), 208 (2), 207 (4), 180 (3), 179 (4), 165 (2), 152 (5), 151 (7), 150 (3); ν_{max} 2925 (w, br), 1670, 1650, 1595 (s), 1575 (sh), 1520, 1375, 1350, 1330 (s), 1290 (s), 1220, 1095, 930 (s), 830 (sh), 720 (sh), 710 (s, sh) cm^{-1}; ^{1}H-nmr ($CDCl_3$) 8.3-6.8 (m, 7H), 3.1 (s, 6H).

1,5-Dichloroanthraquinone

1,5-Dichloroanthraquinone (2.76 g, 0.01 mole) was refluxed in HMPA (20 ml) for 15 minutes. The reaction was then treated as previously mentioned. The resultant dark red residue (2.81 g) was chromatographed to give four main fractions.

Fraction 1 returned 1,5-dichloroanthraquinone (0.1 g, 4%) as a yellow solid; R_f and mass spectrum were identical with those of the starting material.

Fraction 2 yielded, after crystallization (ethanol), 1-chloro-5-methylaminoanthraquinone (0.92 g, 34%) as blood red needles, m.p. 198-200° (lit.[22], 194-197°; lit.[23], 196-197°); mass spectrum m/e 273 (M^+ ^{37}Cl) (33), 271 (M^+) (100%), 270 (34), 256 (15), 254 (43), 245 (3), 243 (10), 236 (9), 228 (2), 226 (4), 216 (4), 215 (5), 214 (10), 201 (2), 199 (5), 188 (4), 186 (9), 180 (6), 165 (4), 164 (6), 163 (6), 152 (11), 151 (14), 150 (13), 136.5 (M, ^{37}Cl)$^{++}$ (4), 135.5 (M^{++}) (9); ν_{max} 3300 (w, br), 2920 (w, br), 1673 (s), 1630 (s), 1600 (s), 1575 (s), 1515 (s), 1425 (sh), 1405 (sh), 1366, 1325 (s), 1260 (s, br), 1205 (sh), 1175, 1005 (sh), 812 (s), 762 (sh), 740 (sh), 710 (sh) cm^{-1}; ^{1}H-nmr ($CDCl_3$) 9.5 (br s, 1H), 8.3-7.0 (m, 6H), 3.0 (d, J = 5.1 Hz, 3H);

^{1}H-nmr ($CDCl_3$ + D_2O) 9.5 (br s, 1H), 8.3-7.0 (m, 6H), 3.0 (skewed d, 3H). Fraction 3 gave, after crystallization (ethanol), 1-chloro-5-dimethylaminoanthraquinone (0.04 g, 1.4%) as brick-red needles, m.p. 153-155° (lit.[23], 144-145°); mass spectrum m/e (M^+ ^{37}Cl) (27), 285 (M^+) (73), 284 (15), 272 (32), 270 (100%), 268 (80), 258 (8), 256 (26), 254 (20), 233 (20), 201 (5), 199 (14), 188 (5), 186 (11), 152 (15), 151 (24), 150 (32), 149 (23); ν_{max} 2860 (br), 1665 (s, sh), 1635 (s), 1590 (s), 1500 (sh), 1425 (s), 1370, 1343, 1300, 1255 (s), 1192, 1157, 1125, 1065 (sh), 1035 (sh), 940 (sh), 910, 810, 793 (s, sh), 750, 720, 705 (s, sh) cm^{-1}; ^{1}H-nmr ($CDCl_3$) 8.2-7.1 (m, 6H), 3.0 (s, 6H). Fraction 4 gave, on evaporation, what is thought to be 1-methylamino-5-dimethylaminoanthraquinone (0.058 g, 2%) as a dark red solid, m.p. 90-96° (lit. m.p. not available[23]); mass spectrum m/e 281 (M^+ ^{13}C) (7), 280 (M^+) (35), 279 (6), 265 (17), 263 (31), 251 (5), 248 (14), 236 (4), 234 (5), 220 (4), 180 (3), 165 (5), 152 (6), 151 (5), 140 (M^{++}) (8), 117 (13), 104 (9), 91 (19), 78 (100%); ν_{max} 3280 (w), 2920 (w, br), 1635, 1625, 1590, 1570, 1510, 1425 (sh), 1400 (sh), 1360, 1315, 1255 (s), 1193, 1175, 1080 (sh), 1035, 960 (sh), 860 (sh), 800, 790, 765, 715 (sh) cm^{-1}; ^{1}H-nmr ($CDCl_3$) 9.6 (br s, 1H), 8.2-6.9 (m, 6H), 3.0 (br s, 9H); ^{1}H-nmr ($CDCl_3$ + D_2O) singlet at δ 9.6 disappears.

1,8-Dichloroanthraquinone

1,8-Dichloroanthraquinone (2.76 g, 0.01 mole) was refluxed in HMPA (20 ml) for 15 minutes and worked up as previously. Chromatography of the resultant black tarry residue, followed by crystallization (ethanol) gave five components.

Fraction 1 was found to be slightly impure 1,8-dichloroanthraquinone (0.11 g, 4%) by t.l.c. and mass spectrum.

Fraction 2 yielded 1-chloro-8-methylaminoanthraquinone (0.7 g, 26%) as red needles with a golden lustre, m.p. 190-193° (lit.[23], 187°); mass spectrum m/e 273 (M^+ ^{37}Cl) (26), 271 (M^+) (92), 270 (7), 256 (31), 254 (100%), 243 (6), 242 (5), 236 (4), 226 (4), 219 (15), 216 (3), 215 (3), 214 (7), 201 (3), 199 (8), 186 (8), 180 (6), 163 (5), 152 (10), 151 (8.5), 150 (9), 135.5 (M^{++}) (2); ν_{max} 3300 (w), 2900 (w, br), 1675 (sh), 1640 (s), 1595 (s), 1580, 1518 (s), 1430, 1320 (s, br), 1250 (s, br), 1180, 1005 (sh), 840 (sh), 790, 740 (s), 600 (br) cm^{-1}; ^1H-nmr ($CDCl_3$) 9.5 (br s, 1H), 8.3-6.9 (m, 6H), 3.0 (d, J = 5.1 Hz, 3H); ^1H-nmr ($CDCl_3$ + D_2O), spectrum remains basically intact.

Fraction 3 was found to contain a mixture (t.l.c.) and was rechromatographed on a microcolumn to yield mainly 1,8-bis-(methylamino)-anthraquinone (0.022 g, 1%) as dark purple micro-crystals, m.p. 198-202° (lit.[22], 215-217°). These were not further purified; mass spectrum m/e 267 (M^+ ^{13}C) (17), 266 (M^+) (100%), 237 (23), 236 (10), 234 (9), 233 (11), 220 (16), 209 (6), 208 (6), 195 (6), 180 (12), 167 (8), 165 (12), 152 (16), 151 (14), 136 (14), 135 (20); ν_{max} 3325 (w), 2910 (w, br), 2475, 1660 (sh), 1625 (s), 1570, 1515, 1440 (sh), 1425 (sh), 1380, 1365, 1305 (s), 1245 (s, br), 1185, 1080, 1010, 840 (sh), 810, 795, 745 (sh), 420 (br) cm^{-1}; ^1H-nmr ($CDCl_3$) 9.5 (br s, 2H), 7.6-7.0 (m, 6H), 3.0 (d, J = 5.1 Hz, 6H); ^1H-nmr ($CDCl_3$ + D_2O) 7.6-7.0 (m, 6H), 3.0 (s, 6H).

Fraction 4 gave 1-chloro-8-dimethylaminoanthraquinone (0.08 g, 3%) as red-black prisms, m.p. 146-148° (lit.[23], 118-119°); mass spectrum

m/e 287 (M^+ ^{37}Cl) (14), 285 (M^+) (38), 284 (5), 270 (48), 268 (100%), 255 (4), 253 (10), 233 (44), 201 (5), 199 (12), 188 (4), 186 (8), 152 (11), 151 (20), 150 (18.6), 142.5 (M^{++}) (5); ν_{max} 2900 (w, br), 1665, 1640 (s), 1580 (s), 1500, 1445 (sh), 1430, 1420, 1375 (sh), 1305 (s), 1255 (s), 1220 (s), 1200, 1127, 1080 (sh), 1065 (sh), 1030 (sh), 947 (s, sh), 900, 825 (sh), 778 (sh), 725 (s) cm^{-1}; ^1H-nmr ($CDCl_3$) 8.2-7.3 (m, 6H), 3.0 (s, 6H).

Fraction 5 afforded a small amount of a red-black solid. This was found to be 1-methylamino-8-dimethylaminoanthraquinone (0.021 g, 1%), m.p. 119-124° (lit. m.p. not available[107]). Crystallization of this material was not attempted; mass spectrum m/e 281 (M^+ ^{13}C) (18), 280 (M^+) (62), 266 (22), 265 (100%), 263 (17), 262 (39), 249 (11), 248 (19), 247 (14), 236 (11), 233 (10), 223 (8), 220 (12), 180 (8), 165 (10), 152 (14), 151 (10), 140 (M^{++}) (26), 132.5 $(M-CH_3)^{++}$ (22), 132 (19), 78 (78); ν_{max} 3300 (w, br), 2930 (br), 1660, 1620 (s), 1580, 1540, 1515, 1320, 1300, 1245, 1225, 1080, 1065, 975, 890, 840 (sh), 780, 745, 670 (w, br) cm^{-1}; ^1H-nmr ($CDCl_3$) 9.5 (br s, 1H), 8.2-6.8 (m, 6H), 3.0 (d, J = 5.1 Hz, 3H), 3.0 (s, 6H); ^1H-nmr ($CDCl_3$ + D_2O), singlet at δ 9.5 disappears.

Reaction with hexaethylphosphoramide (HEPA)

1-Chloroanthraquinone

1-Chloroanthraquinone (0.5 g, 0.002 mole) and HEPA (7 ml) were refluxed for 15 minutes. The reaction mixture was cooled to room temperature and then poured into water (100 ml). The resulting precipitate was collected by filtration and air-dried to yield a reddish-

purple residue (0.42 g). Initial chromatography (chloroform) gave a red mixture (0.22 g). This was rechromatographed to give three fractions.

Fraction 1 gave a small amount of a reddish-purple solid which was found (mass spec.) to contain some 1-chloroanthraquinone plus a compound with M^+ at m/e 313 which contained no chlorine (isotopic ratio). It was not an original or derived impurity of the starting material. The small sample size allowed no further collection of data and no tentative structure could be assigned on the basis of available data.

Fraction 2 was identified as 1-chloroanthraquinone (0.15 g, 30%); R_f and mass spectrum were identical with those of the starting material.

Fraction 3 gave, after careful evaporation, 1-ethylaminoanthraquinone (0.05 g, 10%) as fine red needles, m.p. 110-115° (lit.[108], 119°). It was found to be contaminated (mass spec.) with a small amount of 1-chloroanthraquinone; mass spectrum m/e 252 (M^+ ^{13}C) (9), 251 (M^+) (50), 250 (M-H) (3), 236 ($M-CH_3$) (100%), 222 ($M-C_2H_5$) (2), 208 ($M-CH_3-CH_2N$) (9), 180 ($M-CH_3-CH_2N-CO$) (16), 151 (15), 150 (8), 125.5 (M^{++}) (3), 77 ($C_6H_5^+$) (11), 76 ($C_6H_4^+$) (16), 75 ($C_6H_3^+$) (10); ν_{max} 2930, 2855, 1665, 1630 (sh), 1595 (sh), 1505 (br), 1305 (br), 1270 (s), 1175, 1150, 1075 (sh), 1013, 800, 735 (sh), 707 (sh) cm^{-1}; ^1H-nmr ($CDCl_3$) 9.6 (br s, 1H), 8.3-6.9 (m, 7H), 3.36 (amine doublet superimposed on methylene quartet, J_{HN-CH} = 5.0 Hz, J_{HC-CH} = 7.2 Hz, 2H), 1.4 (t, J = 7.5 Hz, 3H); ^1H-nmr ($CDCl_3$ + D_2O) 8.3-6.9 (m, 7H), 3.36 (q, J = 7.2 Hz, 2H), 1.4 (t, J = 7.5 Hz, 3H).

2-Chloroanthraquinone

2-Chloroanthraquinone (0.5 g, 0.002 mole) was refluxed in HEPA (7 ml) for 15 minutes. The reaction mixture was then treated as previously, yielding a reddish-orange powder (0.43 g). This was found (mass spectrum) to contain mainly starting material as well as a small amount of substituted product. Extraction with ether (3 x 5 ml) gave an orange-yellow solid and an ethereal solution.

The solid was unchanged 2-chloroanthraquinone (0.41 g, 82%); R_f and mass spectrum were identical with those of the starting material.

The ethereal solution was concentrated and separated into its three main components by preparative t.l.c. (silica gel/chloroform). This provided enough sample for mass spectral analysis only.

Fraction 1 was found to be 2-chloroanthraquinone; the mass spectrum was identical with that of the starting material.

Fraction 2 was assigned the structure 2-diethylaminoanthraquinone on the basis of its mass spectrum; m/e 280 (M^+ ^{13}C) (8), 279 (M^+) (41), 265 (M + 1 $-CH_3$)(8), 264 (M-CH_3)(100%), 236 (M-CH_3-C_2H_4) (27).

Fraction 3 (which occurred in comparable proportion to fraction 2) was identified as 2-ethylaminoanthraquinone on the basis of the mass spectrum; m/e 252 (M^+ ^{13}C) (21), 251 (M^+) (100%), 250 (M-H) (88), 236 (M-CH_3) (9); metastable observed at m/e 249, assigned to $[M]^+ \longrightarrow [M-H]^+ + H^\cdot$ (m^*_{obs}: m/e 249; m^*_{calc}: m/e 249.004).

The reaction of various other halo-aromatic compounds with HMPA

A. 4-Chloronitrobenzene

4-Chloronitrobenzene (1.57 g, 0.01 mole) was refluxed in HMPA (10 ml) for 30 minutes. The reaction mixture was allowed to cool to room temperature and slowly poured into cold water (100 ml). The resulting precipitate was collected by suction filtration and air-dried to yield a golden-yellow solid (1.1 g). This was chromatographed (chloroform) to give 4-dimethylaminonitrobenzene (0.5 g, 30%) as bright yellow needles (ethanol), m.p. 163-164° (lit.[109], 163-166°); mass spectrum m/e 166 (M^+) (100%), 165 (M-H) (30), 150 (4), 136 (38), 119 (63), 105 (39), 91 (21), 77 (41); ^{1}H-nmr ($CDCl_3$) 7.3 (a_2b_2 quartet, J = 9.5 Hz, 4H), 3.1 (s, 6H).

4-Bromonitrobenzene

4-Bromonitrobenzene (2.02 g, 0.01 mole) was treated as above with HMPA (10 ml) for 15 minutes. The reaction mixture was treated as previously to give an olive-green solid (1.5 g). Chromatography (chloroform) yielded 4-dimethylaminonitrobenzene (0.6 g, 26%); m.p. and spectra were identical with those of the previously obtained sample.

4-Fluoronitrobenzene

The experiment was repeated using 4-fluoronitrobenzene (1.41 g, 0.01 mole) in HMPA (10 ml) with a 45 minute reflux time. On cooling, the reaction mixture was filtered to give bright yellow spikes of 4-dimethylaminonitrobenzene (0.76 g, 46%) which were identical with previously obtained samples. The filtrate was diluted with water (100 ml) and the resulting precipitate collected by suction filtration. This gave an additional amount of the same compound as bright yellow needles (ethanol) (0.71 g, 43%). Total yield of 4-dimethylaminonitrobenzene was 89%.

B. 2,4-Dinitrochlorobenzene

The reaction was repeated using 2,4-dinitrochlorobenzene (2.02 g, 0.01 mole) and refluxing for 20 minutes. Chromatography (chloroform) gave 2,4-dinitrodimethylaminobenzene (1.1 g, 52%) as orange-yellow spikes (ethanol), m.p. 87-88° (lit.[110], 87°); mass spectrum m/e 211 (M^+) (100%), 194 (88), 166 (35), 164 (29), 148 (44), 136 (82), 119 (68), 106 (29), 91 (29), 78 (41), 77 (38); ^{1}H-nmr ($CDCl_3$) 8.75 (d, J = 2.8 Hz, 1H), 8.25 (doublet of doublets, J_{ortho} = 9.4 Hz, J_{meta} = 2.9 Hz, 1H), 7.1 (d, J = 9.5 Hz, 1H), 3.1 (s, 6H).

2,4-Dinitrofluorobenzene

The experiment was repeated with 2,4-dinitrofluorobenzene (1.86 g, 0.01 mole), refluxing for 25 minutes. Standard work-up of the reaction gave 2,4-dinitrodimethylaminobenzene (1.7 g, 81%), identical with the previously obtained sample.

C. 2-Chloronitrobenzene

2-Chloronitrobenzene (1.57 g, 0.01 mole) and HMPA (10 ml) were refluxed for 20 minutes. After cooling, the mixture was diluted with water (100 ml). On standing, an organic phase separated from the aqueous layer and was removed using a separatory funnel. The resulting orange-brown liquid was taken up in chloroform, the solution was dried ($MgSO_4$) and the solvent removed on a rotary evaporator. Chromatography of this crude liquid gave 2-dimethylaminonitrobenzene (0.45 g, 27%) as a yellow-orange oil; mass spectrum m/e 166 (M^+) (71), 165 (13), 149 (76), 133 (10), 121 (48), 119 (62), 105 (51), 104 (56), 91 (100%), 77 (71); ^{1}H-nmr ($CDCl_3$) 7.8-6.7 (m, 4H), 2.9 (s, 6H); the amine was characterized as the picrate, yellow microcrystals (ethanol) m.p. 99-100° (lit.[111], 102-103.5°).

3-Chloronitrobenzene

The above reaction was repeated using 3-chloronitrobenzene (1.57 g, 0.01 mole) with a 30 minute reflux time. Standard work-up gave a dark brown solid (0.47 g). Chromatography gave two fractions.

Fraction 1, after crystallization from ethanol/ether gave 3,3'-dichloroazobenzene (0.04 g, 2%) as orange needles, m.p. 102-103° (lit.[112], 101°); mass spectrum m/e 254 (M^+ $2^{37}Cl$) (2), 252 (M^+ ^{37}Cl) (14), 250 (22), 222 ($M-N_2$) (0.3), 186 ($M-N_2-HCl$) (1.2), 151 ($M-N_2-HCl-Cl$) (5), 138 ($C_6H_3ClN_2^+$) (17), 126 ($C_5H_3ClN_2^+$) (1.4), 111 ($C_6H_4Cl^+$) (100%), 75 ($C_6H_3^+$) (43); ν_{max} 1580, 1560 (N=N), 1455, 1410, 1295, 1190 (s), 1060, 880 (s, sh), 785 (s, sh), 680 (s, sh) cm^{-1}; ^{1}H-nmr ($CDCl_3$) 8.0-7.2 (m).

Fraction 2 was identified as 4-dimethylaminonitrobenzene (0.0075 g, 0.5 %); m.p. and mass spectrum were identical with those of previously obtained samples.

A large amount of dark brown material which could not be eluted was retained on the column.

4-Chloroaniline

The experiment was repeated using 4-chloroaniline (1.27 g, 0.01 mole) and refluxing for 1 hour.

Standard work-up gave a quantitative return of 4-chloroaniline, mass spectrum and R_f were identical with those of the starting material.

The reaction of substituted phenols with HMPA

4-Nitrophenol

4-Nitrophenol (1.39 g, 0.01 mole) was refluxed in HMPA (10 ml) as in previous experiments for 30 minutes. The mixture was cooled, poured into water (100 ml) and filtered. The resulting residue was air-dried and then chromatographed (chloroform) to yield 4-dimethylaminonitrobenzene (0.5 g, 30%) as bright yellow needles. It was identical with previously obtained samples.

2-Nitrophenol

2-Nitrophenol (1.39 g, 0.01 mole) was treated as in the preceding experiment. After the reaction mixture cooled, it was poured into

water (200 ml) and a steam distillation was carried out. The distillate was collected until it became colourless. The resulting aqueous solution was extracted with chloroform (3 x 50 ml), dried (Na_2SO_4) and the solvent removed to give 2-dimethylaminonitrobenzene (0.3 g, 18%) as an orange-yellow oil which was identical with the previously obtained sample.

2,4-Dinitrophenol

2,4-Dinitrophenol (1.84 g, 0.01 mole) was treated as previously with HMPA (10 ml) for 20 minutes.

Standard work-up followed by chromatography (chloroform) gave 2,4-dinitrodimethylaminobenzene (1.25 g, 59%) as orange-yellow needles which were identical with previously obtained samples.

Pentachlorophenol

Pentachlorophenol (2.66 g, 0.01 mole) was refluxed in HMPA (10 ml) for 15 minutes. Standard work-up gave a cream-coloured solid which was twice crystallized from ethanol/water to give pentachlorophenyl-tetramethylphosphorodiamidate (CVII) (2.65 g, 67%) as off-white flakes, m.p. 145-147°; (Calcd. for $C_{10}H_{12}Cl_5N_2PO_2$: C, 29.99; H, 3.02; H, 7.00; P, 7.73. Found. C, 30.19; H, 3.15; N, 7.10; P, 7.43.); mass spectrum m/e 402 (M^+ $2^{37}Cl$) (2), 400 (M^+ ^{37}Cl) (4), 298 (M^+) (3), 367 (20), 365 (39), 363 (M-Cl) (30), 358 (3), 356 (5), 354 (M-NMe_2) (3), 268 (5), 266 (7), 264 ($C_6HCl_5O^+$) (5), 239 (6), 237 (7), 235 ($C_6HCl_5O^+$-COH) (5), 169 (2), 167 (6), 165 ($C_6HCl_5O^+$-COH-2Cl) (6), 135 ($C_4H_{11}N_2PO^+$) (100%); ν_{max} 2800 (br), 1530, 1480, 1460, 1380 (br),

1355, 1305 (br), 1210 (br), 1180, 1130 (sh), 1075 (sh), 980 (br, s), 820 (br, s), 760 (sh), 740 (sh), 710, 670, 485, 460 cm^{-1}; ^{1}H-nmr ($CDCl_3$) 2.8 (d, J = 10.3 Hz); ^{31}P-nmr ($CHCl_3$) 15.2 (m, $\bar{J}$ = 9.9 Hz); using broad base decoupling the multiplet collapses to a singlet at δ 15.2.

Attempted Rearrangement of the Phosphorodiamidate

The isolated phosphorodiamidate (0.5 g, 0.00125 mole) was refluxed in HMPA for 1 hour. The cooled reaction mixture was poured into water (100 ml) and an off-white solid collected by suction filtration. Crystallization (carbon) from ethanol/water gave pentachlorophenyl-tetramethylphosphorodiamidate (0.22 g, 44%) as white needles, m.p. and mass spectrum identical with those of the starting material. There was no evidence for even a trace of N,N-dimethyl-pentachloroaniline (CVIII).

REFERENCES

1. J.F. Bunnett, J. Chem. Educ., 38, 278 (1961).

2. R.W. Hoffman, Dehydrobenzene and Cycloalkynes, Academic Press, New York (1967).

3. G. Hall, R. Piccolini and J.D. Roberts, J. Amer. Chem. Soc., 77, 4540 (1955).

4. R. Benkeser and W. Buitng, J. Amer. Chem. Soc., 74, 3011 (1952).

5. E. Dreher and R. Otto, Annalen, 154, 93 (1870).

6. R. Stoermer and B. Kahlert, Berichte, 35, 1633 (1902).

7. (a) J.D. Roberts, H. Simmons, L. Carlsmith and C. Vaughan, J. Amer. Chem. Soc., 75, 3290 (1953).
   (b) J.D. Roberts, D. Semenow, H. Simmons, L. Carlsmith, J. Amer. Chem. Soc., 78, 601 (1956).

8. F. Bergstrom, R.E. Wright, C. Chandler and W.A. Gilkey, J. Org. Chem., 1, 170 (1936).

9. J.D. Roberts, C. Vaughan, L. Carlsmith and D. Semenow, J. Amer. Chem. Soc., 78, (1956).

10. K.E. Hamlin and A.W. Weston, Org. Reactions, 9, 1 (1957).

11. J.F. Bunnett and J.A. Skorcz, J. Org. Chem., 27, 3836 (1962).

12. G. Wittig and G. Steinhoff, Annalen, 676, 21 (1964).

13. J.F. Bunnett, T. Kato, R.R. Flynn and J.A. Skorcz, J. Org. Chem., 28, 1 (1963).

14. R. Huisgen and J. Sauer, Angew. Chem., 72, 91 (1960).

15. B.F. Hrutfiord and J.F. Bunnett, J. Amer. Chem. Soc., 80, 2021 (1958).

16. B.F. Hrutfiord and J.F. Bunnett, J. Amer. Chem. Soc., 80, 4745 (1958).

17. J.F. Bunnett and B.F. Hrutfiord, J. Amer. Chem. Soc., 83, 1691 (1961).

18. T. Kato and J.F. Bunnett, unpublished work.

19. G.J. Chen and M.S. Gibson, J. Chem. Soc. Perkin I, 1138 (1975).

20. M.S. Gibson, S.M. Vines and J.M. Walthew, J. Chem. Soc. Perkin I, 155 (1975).

21. M.L. Kaldas, M.Sc. Thesis, Brock University (1974).

22. R.H. Hall and D.H. Hey, J. Chem. Soc., 736 (1948).

23. W.M. Lord and A.T. Peters, J. Chem. Soc. (C), 783 (1968).

24. J. Griffiths and C. Hawkins, J. Chem. Soc. Perkin I, 2283 (1974).

25. W.M. Lord and A.T. Peters, J. Chem. Soc. (C), 21, 3600 (1971).

26. W.M. Lord and A.T. Peters, J. Chem. Soc. Perkin I, 2305 (1973).

27. G. Philip and S.V. Sunthankar, Chem. and Ind., 433 (1975).

28. D.G. Davies and P. Hodge, J. Chem. Soc. (C), 19, 3158 (1971).

29. D.G. Davies, P. Hodge and P. Yates, J. Chem. Soc. Perkin I, 2299 (1973).

30. G.J. Chen, M.Sc. Thesis, Brock University (1973).

31. D.G. Davies, M. Derenberg and P. Hodge, J. Chem. Soc. (C), 3, 455 (1971).

32. A. Korczynski, Bull. soc. chim., [4] 35, 1186 (1924).

33. L.F. Fieser and J.L. Hartwell, J. Amer. Chem. Soc., 57, 1482 (1935).

34. H.W. Moore and H.R. Sheldon, J. Org. Chem., 33, 4019 (1968).

35. D. Misiti, H.W. Moore and K. Folkers, Tet. Letters, 1071 (1965).

36. D. Misiti, H.W. Moore and K. Folkers, Tetrahedron, 22, 1201 (1966).

37. R.W. Rickards and R.M. Smith, Tet. Letters, 2361 (1966).

38. G.R. Bedford, G. Jones and B.R. Webster, Tet. Letters, 2367 (1966).

39. G. Jones, J. Chem. Soc. (C), 1808 (1967).

40. P.A.S. Smith, Molecular Rearrangements, 1, 507, P. deMayo (ed.), Interscience, New York (1963).

41. A. Berger, A. Loewenstein and S. Meiboon, J. Amer. Chem. Soc., 81, 62 (1959).

42. A. Michaelis, Annalen, 326, 129 (1903).

43. H. Normant, Angew. Chem. internat. Edit., 6, 1046 (1967).

44. J. Schafer and C. Curran, Inorg. Chem., 4, 623 (1965).

45. G. Fraenkel, S.H. Ellis and D.T. Dix, J. Amer. Chem. Soc., 87, 1406 (1965).

46. R.L. Heider, Chem. Abstracts, 47, 4900 (1953).

47. J. Kopechy and J. Smejkal, Chem and Ind., 36, 1529 (1966).

48. R.S. Monson, Tet. Letters, 567 (1971).

49. R.S. Monson and D.S. Priest, Chem. Comm., 1018 (1971).

50. J. Bourdais and Cl. Mahieu, C. R. hebd. Séances Acad. Sci., Ser. C, 263, 84 (1966).

51. H. Mauss and F. Mietzsch, Klin. Wochschr., 12, 1276 (1933); cf. G.M. Badger, The Chemistry of Heterocyclic Compounds, Academic Press, New York (1961) p. 359.

52. D.J. Dupré and F.A. Robinson, J. Chem. Soc., 549 (1945).

53. H.F. Hodson, J.F. Batchelor and J.H. Gorvin, Brit. Appl., 41, 852 (1973).

54. R.M. Acheson, An Introduction to the Chemistry of Heterocyclic Compounds, Interscience, New York (1960) pp. 242-3.

55. M.S. Khan, J.R. Lewis and R.A. Watt, Chem. and Ind., 744 (1975).

56. S. Coffey, Chem. and Ind., 1068 (1953).

57. J.C.E. Simpson, C.M. Atkinson, K. Schofield and O. Stephenson, J. Chem. Soc., 646 (1946).

58. A. Eckert and K. Steiner, Monatsh., 35, 1129 (1914).

59. J.H. Adams, P. Gupta, M.S. Khan, J.R. Lewis and R.A. Watt, J. Chem. Soc. Perkin I, 2089 (1976).

60. E. LeGoff, J. Amer. Chem. Soc., 84, 3975 (1962).

61. J.H. Clark and J.M. Miller, Chem. Comm., 229 (1976).

62. I.H. Bowen, P. Gupta, M.S. Khan and J.R. Lewis, J. Chem. Soc. Perkin I, 2524 (1972).

63. R.I. Fryer, J. Earley and L.H. Sternbach, J. Chem. Soc., 4979 (1963).

64. Brit. Pat., cf. N.N. Vorozhtov, MTP International Review of Science, Organic Chemistry Series One, Aromatic Compounds, vol. 3, p. 331, H. Zollinger (ed.), Butterworth & Co., London (1973).

65. M. Ballester and S. Olivella, Polychloroaromatic Compounds, p. 27, H. Suschitsky (ed.), Plenum Press, New York (1974).

66. A. Green, J. Chem. Soc., 2203 (1926).

67. A. Goldberg and A. Wragg, J. Chem. Soc., 4227 (1958).

68. H.E. Fierz-David, Helv. Chim. Acta, 10, 210 (1927).

69. J. Miller and A.J. Parker, Austral. J. Chem., 83, 117 (1961).

70. L. Horner and A. Christman, Chem. Ber., 96, 388 (1963).

71. G.J. Marriott and R. Robinson, J. Chem. Soc., 134 (1939).

72. H. Decker and E. Laube, Annalen, 348, 231.

73. H. Decker and A. Würsch, Annalen, 348, 239.

74. E. Beckmann and O. Liesche, Berichte, 56, 1 (1923).

75. G. Caronna and S. Palazzo, Gazz. chim. ital., 83, 533 (1953).

76. G. Caronna and S. Palazzo, Gazz. chim. ital., 84, 1135 (1954).

77. L. Rand and R.J. Dolinski, J. Org. Chem., 30, 48 (1965).

78. L. Rand, W. Wagner, P.O. Warner and L.R. Kovac, J. Org. Chem., 27, 1034 (1962).

79. M. Fischer and F. Wagner, Chem. Ber., 102, 3486 (1969).

80. J. Nasielski and G. Jacqmin, Tetrahedron, 28, 597 (1972).

81. E.P. Fokin and V.V. Russkikh, Izvest. Sibirsk. Otdel. Akad. Nauk., Ser. Khim. Nauk., 126 (1965).

82. E.P. Fokin and V.V. Russkikh, Zhur. Org. Khim., 2, 907 (1966).

83. E.P. Fokin and V.V. Russkikh, Zhur. Org. Khim., 2, 912 (1966).

84. J. Lynch and O. Meth-Cohn, J. Chem. Soc. Perkin I, 920 (1973).

85. I.G. Farbenindustrie, Fortschritte der Teerfabrikation und verwandter Industriezweige, 16, 1189.

86. L.S. Kobrina, Fluorine Chem. Reviews, vol. 7, p. 5, P. Tarrant (ed.), Marcel Dekker, Inc., New York (1974).

87. E. Zaugg and A.D. Schaefer, Anal. Chem., 36, 2121 (1964).

88. Bayer & Co., Chem. Zentr. (II), 1372 (1902).

89. J.H. Boyer, Nitrenes, p. 170, W. Lwowski (ed.), Interscience, New York (1970).

90. C.D. Gutsche and D.J. Pasto, Fundamentals of Organic Chemistry, Prentice-Hall, Inc., New York (1975).

91. E.H. White and C.A. Elliger, J. Amer. Chem. Soc., 87, 5261 (1965).

92. B. Loev and J.T. Massengale, J. Org. Chem., 22, 1186 (1957).

93. A.L. Rocklin, J. Org. Chem., 21, 1478 (1956).

94. J. Duchesne and A. Monfils, J. Chem. Phys., 22, 562 (1954).

95. A.J. Elliott, M.S. Gibson, M.M. Kayser and G.A. Pawelchuk, Can. J. Chem., 51, 4115 (1973).

96. B. Loev, and M.M. Goodman, Chem. and Ind., 2026, (1967).

97. A.J. Gordon and R.A. Ford, The Chemist's Companion, John Wiley & Sons, Inc., New York, (1972).

98. A.I. Vogel, A Textbook of Practical Organic Chemistry, Longmans, Green and Co., (1956)

99. L. Gattermann, Annalen, 393, 169.

100. L. Wacker, Berichte, 35, 3925 (1902).

101. Bayer & Co., Chem. Zentr. (I), 1342 (1902).

102. Bayer & Co., Chem. Zentr. (I), 79 (1902).

103. E. Laube, Berichte, 39, 2245 (1906).

104. F. Ullman and O. Fodor, Annalen, 380, 320 (1911).

105. A. Allais, Ann. Chim. [12] 2, 739 (1947).

106. F. Ullman and R. Medenwald, Berichte, 46, 1801 (1913).

107. Bayer & Co., Chem. Zentr. (II), 750 (1903).

108. Höchster Farbwerken, Chem. Zentr. (II), 41 (1916).

109. D.P. Evans and R. Williams, J. Chem. Soc., 1199 (1939).

110. G. Gallas and A. Alonso, Anales soc. españ. fis. quim., 28, 645 (1930).

111. H.H. Hodgson and A. Kershaw, J. Chem. Soc., 280 (1930).

112. D. Vorländer and G.A. Meyer, Annalen, 320, 129 (1902).

113. M.S. Gibson and M. Kayser, unpublished results (Brock University).